American Journal of Diseases of Children

VOLUME 43 JANUARY, 1932 NUMBER 1

GUANIDINE AS A FACTOR IN ALIMENTARY INTOXICATION IN INFANTS *

KATHARINE DODD, M.D.

A. S. MINOT, PH.D.

AND

HORTON CASPARIS, M.D.

NASHVILLE, TENN.

The incidence of diarrhea and vomiting in infants during the summer months has considerably decreased with better methods of feeding and a more sanitary milk supply; but summer diarrhea and vomiting are still commonly seen, especially in localities where the heat is extreme. This familiar combination of symptoms has been variously known as cholera infantum, summer complaint or diarrhea, acute gastro-intestinal indigestion, colitis, dyspepsia, decomposition and alimentary intoxication. These names have often included bacillary dysentery as well as the less well understood diarrheas in which no specific infection of the gastro-intestinal tract can be found. In this paper we shall confine ourselves to the nonspecific diarrheas of the severe and frequently fatal type, and for the purpose of discussion we shall refer to the condition as alimentary intoxication.

A great deal of study has been devoted to this condition by various investigators, and although the conclusions are somewhat conflicting it is rather generally admitted that parenteral infection, particularly otitis media and perhaps mastoiditis, summer heat, dehydration and artificial feeding are all important etiologic factors. The infants are prostrated or restless; the fontanels and eyes are sunken; the hands and feet are cold, and without prompt treatment many patients die. The babies usually vomit everything, including water. The stools are innumerable and are large and watery. In the most severe cases the vomitus is brown from the presence of changed blood, and fresh or changed blood is occasionally found in the stools. There is marked suppression of urine or complete anuria. Frequently the respirations are deep, indicating air-hunger. Convulsions may occur as a terminal event.

* Submitted for publication, April 22, 1931.

* From the Department of Pediatrics, Vanderbilt University Medical School.

The chemistry of this condition has been extensively studied (Hartmann,[1] Gamble,[2] Darrow and Buckman[3]). The outstanding changes as reported in these various studies are those secondary to the dehydration and the loss of fixed base in the stools. The total proteins and chlorides of the blood are usually increased, while the base bicarbonates are decreased. Other less constant changes in nonprotein nitrogen, inorganic phosphates and lactic acid have also been observed.

The usual treatment is an attempt to combat any infection present and at the same time to reestablish a more normal salt and fluid equilibrium. Water is given by mouth when possible; dextrose, physiologic solution of sodium chloride or buffer solutions are injected intravenously, intraperitoneally and subcutaneously, and blood is given by transfusion. In extreme cases the administration of alkalis may also be necessary. To avoid aggravating the condition, food is usually temporarily withheld.

Such measures will save a large number of infants. There are, however, a considerable number of cases in which there is only transient improvement, soon followed by death. Powers,[4] in his review of the subject, reported a mortality of 33 per cent, but thought that this could be reduced to not more than 25 per cent under optimum conditions. Hartmann's reports,[1] perhaps because he was working in a hotter climate, give the impression of an even higher mortality. Some of these infants undoubtedly die from the original or intercurrent infections; others are moribund on admission and die before adequate treatment can be given. In certain remaining cases there seems to be some as yet unidentified toxic agent, the action of which apparently persists and prevents recovery even when the infection has subsided and when attempts to maintain acid-base and fluid equilibrium have been continued.

The very hot summer of 1930 produced almost an epidemic of alimentary intoxication in Nashville. Many extremely sick infants were admitted to the hospital, presenting the typical picture described. Although the accepted forms of treatment were used, the results were discouraging. When the infants were brought to the hospital before

1. Hartmann, A. F.: Chemical Changes Occurring in the Body as the Result of Certain Diseases: I. The Effects of Diarrhea, Vomiting, Dehydration and Oliguria on the Acid-Base Balance of the Plasma of Infants with Mastoiditis, Am. J. Dis. Child. **35**:557 (April) 1928.

2. Gamble, J. L.: Acidosis and Alkalosis, New England J. Med. **199**:1318, 1928; Dehydration, ibid. **201**:909, 1929.

3. Darrow, D. C., and Buckman, T. E.: The Volume of the Blood: II. The Volume of the Blood and the Concentration of Crystalloids and Electrolytes in Dehydration and Edema, Am. J. Dis. Child. **36**:248 (Aug.) 1928.

4. Powers, G. F.: A Comprehensive Plan of Treatment for the So-Called Intestinal Intoxication of Infants, Am. J. Dis. Child. **32**:232 (Aug.) 1926.

they were actually moribund, there was usually marked initial improvement following treatment, but this was transient. Many relapsed into acidosis in spite of continued treatment; the diarrhea persisted and vomiting recurred, and a large percentage of the infants of this group died. We became more and more impressed with the idea that we were failing because our treatment did not adequately combat some obscure toxic factor.

This unknown toxic substance could apparently injure almost any tissue. Clinically, in the majority of these infants, there was evidence of acute nephritis. There were casts, albumin and sometimes red blood cells in the urine and a slight retention of nonprotein nitrogen in the blood throughout the illness, with a marked rise shortly before death. In others there was less evidence of damage to the kidney but there were marked symptoms of involvement of the central nervous system. The latter infants had convulsions or twitching of the extremities, their necks were stiff, and there was an increase in globulin and white blood cells in the spinal fluid without evidence of infection. The fact that the vomitus, and occasionally the stools, contained changed blood was in itself evidence of damage to the gastro-intestinal tract.

At autopsy the nonspecific nature of the toxic agent was borne out by the pathologic findings. In the kidneys in many cases there was parenchymatous degeneration and at times infiltration of red blood cells. Frequently the brain was found to be edematous, with occasionally gross subdural hemorrhages but more often minute hemorrhages in the substance of the brain and cord. Fatty or parenchymatous degeneration was present in the liver. There were often hemorrhages in the spleen and sometimes also in the suprarenals and pancreas. The gastro-intestinal tract was congested, and frequently there were petechiae in the stomach and small intestine. Unless death was due to terminal pneumonia, the lungs and heart were apparently normal.

As the epidemic progressed and the inadequacy of our treatment became more apparent, greater emphasis was placed on a search for the probable toxic agent. The clinical picture of bloody vomitus and diarrhea and acidosis associated with nervous hyperexcitability or prostration was superficially so similar to the condition that had been repeatedly observed by Minot and Cutler [5] in animals, in which there was an increased guanidine in the blood, that we were led to look for a similar increase of this toxic substance in our patients.

Since a frequent accompaniment of hyperguanidinemia in intoxicated animals was a severe hypoglycemia, the blood sugar levels were first

5. Minot, A. S., and Cutler, J. T.: Guanidine Retention and Calcium Reserve as Antagonistic Factors in Carbon Tetrachloride and Chloroform Poisoning, J. Clin. Investigation **6**:369, 1928.

studied in infants with alimentary intoxication. In a few instances these values were found to be low, and we were encouraged to take the larger amounts (10 cc.) of blood required for guanidine determinations. Only a few infants with severe alimentary intoxication were admitted to the hospital after this study was started, but in the five cases that are presented concentrations of guanidine were found that are comparable to those found in intoxicated animals.[5]

The method used for the determination of guanidine was that of Major and Weber [6] as slightly modified by Minot and Cutler.[5] These figures were not corrected for creatine by the method outlined in a later paper by Weber.[7] Total creatinine determinations on 5 cc. of the protein-free blood filtrate, however, showed that there was no appreciable rise in creatine or creatinine coincident with the increase in guanidine. When determinations are carried out in this manner the normal guanidine concentration in the blood of children is usually between 0.3 and 0.4 mg. per hundred cubic centimeters of blood. The average normal concentration is about 0.35 mg. These figures are directly comparable to the figures reported by Minot and Cutler [5] in dogs. The guanidine concentration in severely intoxicated dogs varied from 0.6 to 1.5 mg. per hundred cubic centimeters of blood which, as will be seen later, corresponds to the levels reached in toxic children.

The antagonistic action between calcium salts and guanidine has been repeatedly demonstrated (Fuhner,[8] Major and Stephanson,[9] Clarke [10]). The efficiency of calcium treatment in animals with an increase in guanidine in the blood has been described (Minot and Cutler,[5] Minot [11]). Animals receiving calcium previous to or early in the course of the intoxication could be prevented from developing symptoms of poisoning in spite of high guanidine levels in the blood, while animals already severely toxic could often be cured by persistent calcium therapy.

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6. Major, R. H., and Weber, C. J.: The Probable Presence of Increased Amounts of Guanidine in the Blood of Patients with Arterial Hypertension, Bull. Johns Hopkins Hosp. **40**:87, 1927.

7. Weber, C. J.: The Determination of Guanidine Bases in the Blood, Proc. Soc. Exper. Biol. & Med. **24**:712, 1927.

8. Fuhner, H.: Die periphere Wirkung des Guanidines, Arch. f. exper. Path. u. Pharmakol. **58**:1, 1908; Ueber die Guanidinkontractur des Skelettmuskels, Arch. f. exper. Path. u. Pharmakol. **105**:265, 1925.

9. Major, R. H., and Stephanson, W.: Further Studies on the Elevation in the Blood Pressure by Guanidine Poisoning, Bull. Johns Hopkins Hosp. **35**:186, 1924.

10. Clark, G. A.: Interrelation of Parathyroids, Suprarenals and Pancreas, J. Physiol. **58**:294, 1923-1924.

11. Minot, A. S.: Data to be published.

Proceeding on the hypothesis that we might be dealing with a guanidine intoxication in infants, the following few cases were studied from this point of view.

REPORT OF CASES

CASE 1.—An infant of 3 months was admitted to the hospital with a history of respiratory infection followed by diarrhea and vomiting. He was cold and blue and presented all the evidences of extreme dehydration. He was immediately placed in blankets with hot water bottles and was given 5 per cent dextrose solution intravenously and Hartmann's[12] solution intraperitoneally. During the procedure he vomited dark changed blood. The ear drums were incised, and pus was obtained. The child's temperature, which had been 102.5 F., fell to normal, and he looked decidedly better. The vomiting stopped, the diarrhea decreased and a small amount of food was taken. In spite of repeated blood transfusions, the administration of large amounts of fluid orally and parenterally and good drainage from the ears, improvement was not satisfactory. On the sixteenth day there were several large black stools which contained blood. The temperature became subnormal. Another transfusion of blood and the administration of more fluids improved the condition slightly, but on the twenty-first day clonic convulsions and irritability combined with symptoms of acidosis were observed. The blood sugar was found to be 60 mg. per hundred cubic centimeters of blood. This was in accord with the observations in the animal experiments, and as the child had taken little or no calcium in his diet for some time, 5 cc. of 10 per cent calcium gluconate solution was given intramuscularly and 1 Gm. of the salt was given every three hours by mouth. Two days later the guanidine in the blood was determined and was found to be 0.59 mg. per hundred cubic centimeters. The symptoms of peripheral hyperexcitability disappeared, but the child remained spastic. It seemed likely that since there had been gastro-intestinal hemorrhages, there might also have been an intracranial hemorrhage. There were increased globulin and a white cell count of 90 in the spinal fluid, but no organisms could be found in smears or by culture. The symptoms of intoxication continued to improve with continued calcium medication, but the child remained semiconscious and died a week later of terminal pneumonia. At autopsy a large fairly recent subdural hemorrhage was found.

In the first case it is evident from the description that we were late in making a guanidine determination on the blood. From the course of the symptoms we think that the guanidine level in the blood had probably been high for several days before the determination was made. We were encouraged by the improvement in the diarrhea and intoxication to think that the moderately increased guanidine was significant, and it seemed possible that earlier medication with calcium might have saved the child's life.

CASE 2.—A child of 3 months was admitted to the hospital in a state of collapse, similar to that of the patient in case 1, following diarrhea and vomiting of four days' duration. This child also improved under the usual methods of treatment, but the improvement was not continuous and twenty-seven days after admission he was worse than at any time since the first day. Chemical studies at that time showed 1 mg. of guanidine, 77 mg. of sugar and 47 mg. of nonprotein nitrogen

12. Hartmann, A. F.: Acidosis, Alkalosis and Dehydration, Colorado Med. **26**:373, 1929.

per hundred cubic centimeters of blood. Intramuscular medication with calcium gluconate was started at once in doses of from 1 to 2 cc. of 10 per cent solution twice a day. Improvement was gradual but steady. Ten days later the blood chemistry was entirely normal, and the patient was discharged well.

Encouraged by the results of very conservative treatment with calcium in these two infants, we decided to adopt the more vigorous treatment used by Minot and Cutler [5] in their animal experiments. They found the intravenous administration of calcium the only adequate form of therapy for animals already showing symptoms of severe guanidine intoxication.

CASE 3.—In an artificially fed infant of 3 months, who had always done poorly and at the time of admission weighed less than at birth, diarrhea and vomiting developed two days before admission. The infant had otitis media and was extremely dehydrated. After fluids were administered and the ear drums incised, the temperature became normal and the child did fairly well but continued to vomit occasionally and to have several large watery stools a day. His emaciation was so extreme that unless nutrition could be rapidly improved the chances of recovery seemed slight. The blood sugar was observed to be decreasing and reached 66 mg. per hundred cubic centimeters on the third day. The guanidine concentration was 0.44 mg. per hundred cubic centimeters, but by the next day it increased to 0.55 mg. Since this was only a moderate increase in guanidine, calcium was given intramuscularly at first. Vomiting ceased for several days, but the condition of the infant remained practically unchanged. Nine days later, vomiting recurred and the diarrhea increased. The blood sugar was found to be 58 mg. and the guanidine concentration, 0.86 mg. per hundred cubic centimeters of blood. Two cubic centimeters of 10 per cent calcium gluconate was given intravenously in 100 cc. of 5 per cent dextrose solution. The intramuscular administration of 2 cc. of 10 per cent calcium gluconate twice a day was also continued. The vomiting ceased and did not recur. The diarrhea disappeared more gradually. The infant's appetite improved, and he began to gain weight steadily. The intravenous injection of calcium was repeated for the first few days, and the intramuscular administration was continued for three weeks. At discharge, the guanidine concentration in the blood was normal.

CASE 4.—An infant of 7 weeks was sent to the hospital with a diagnosis of marasmus. His mother had died at his birth, and he had been fed one artificial formula after another until he refused all food; he had marked diarrhea and weighed only 5½ pounds (2.5 Kg.). Except for extreme emaciation the only pathologic finding on admission was the presence of casts in the urine. The infant was put on a diet of skimmed milk, cane sugar and egg yolk, and gained consistently until otitis media developed on the sixteenth day after admission. He began to vomit and had from six to nine thin, watery stools a day. The number of casts in the urine increased greatly, and there was considerable albuminuria. In two days he lost all the weight that he had gained while in the hospital. Some improvement followed incision of the ear drums, administration of fluids and a transfusion of blood, but it was only transient and he began to lose weight rapidly. A guanidine concentration of 0.87 mg., nonprotein nitrogen of 48 mg. and blood sugar of 64 mg. per hundred cubic centimeters of blood were found at this time. The child was treated with calcium gluconate administered intravenously, intra-

muscularly and orally. The vomiting ceased, and the stools became firm in consistency. He gained weight almost daily until the time of discharge when he weighed 8 pounds (3.6 Kg.). At discharge the blood chemistry and the urine had become normal. When this infant was seen three months later he was in excellent condition.

CASE 5.—A fairly well nourished child of 9 months was admitted to the hospital with a history of having done well during the first seven months of life while she was breast fed. On artificial formulas she had always had mild diarrhea, but had continued to gain until two weeks before admission when a respiratory infection developed. The diarrhea became worse, and she began to vomit. She gradually refused to eat and finally refused even water. She became dehydrated. On admission she was given water by mouth every hour. As she took this well and did not vomit, feeding was started in small amounts on the second day. On the third day the temperature rose to 103 F. and she was found to have otitis media. Fluids were given intraperitoneally and subcutaneously, but she soon began to vomit again, to have thin, watery stools and to lose weight rapidly. The blood sugar was found to be 71 mg. and the guanidine 0.53 mg. per hundred cubic centimeters of blood. Since this was only a moderate increase in guanidine, she was given 2 cc. of calcium gluconate intramuscularly twice a day, but she continued to lose weight rapidly. Two days after the previous determination the guanidine concentration was 1.2 mg. per hundred cubic centimeters of blood. Intravenous medication with calcium consisting of 4 cc. of 10 per cent calcium gluconate was given, and the intramuscular administration of calcium was continued. The vomiting stopped, the stools became more firm and the child rapidly regained her lost weight. Four days later the guanidine concentration was normal. She seemed to have recovered from the alimentary intoxication when unfortunately rapidly fatal bronchial pneumonia with suppurative pleurisy developed. At autopsy, besides pneumonia, there were found fatty degeneration of the liver, congestion of the gastro-intestinal mucosa and focal hemorrhages in the suprarenals.

COMMENT

The number of our cases is obviously too small to warrant any conclusions. As the study of infants from the point of view of guanidine intoxication was begun toward the end of the summer, we have not yet been able to collect more data and are therefore publishing these results as a preliminary report. We believe, however, that we have a definite indication that guanidine or guanidine-like substances may be toxic agents that led to some of the poor results that we have had in the treatment of summer diarrheas in spite of our following accepted procedures. If this is true, the administration of calcium should prove a valuable addition to the present methods of treatment. Had we used the calcium as a preventive measure at the time when we obtained the initial improvement from the administration of fluids, and had we administered calcium intravenously more promptly whenever marked symptoms of intoxication developed, it appears possible that there would have been fewer deaths.

As yet the source or the fate of guanidine in the body is not known. Because of the presence of the guanidine group in the amino-acid arginine and in creatine, one thinks, of course, that these substances may be interrelated. However, nothing definite is known regarding the details of such a relationship. Except for slight traces, guanidine appears to be a pathologic constituent of the blood. The colorimetric method used does not distinguish between different forms of guanidine. We may be dealing with simple guanidine or with the more toxic methyl guanidine or even with more complicated products. Our evidence that we are dealing with guanidine intoxication rests partly on results obtained by this color reaction which is none too specific. More definite evidence is furnished by the striking similarity of the symptoms and tissue changes (to be discussed in a subsequent paper) seen in infants to those produced by experimental guanidine poisoning, and by the similarity of response to calcium in the infants and the experimental animals.

Investigations in the past have associated guanidine increase with injury to the liver (Minot and Cutler,[5] Ellsworth [13]) and with parathyroid deficiency (Paton and Findlay [14]). In the cases reported there is no indication that either of these factors is primary. Studies now in progress [15] seem to indicate that necrotic or autolyzing tissue of various types may serve as a source of guanidine. The relation that this may have to severe dehydration can be proved only by further investigation.

The clinical results as well as those of animal experiments seem to indicate that the efficacy of calcium lies in its antagonistic action to guanidine. In animal experiments it has been repeatedly demonstrated that one is not dealing with a hypocalcemia but rather with an apparent need for extra calcium due to the presence of guanidine. The guanidinemia is not influenced by the treatment. In fact, in some instances the level continues to rise for a day or two even when considerable relief from symptoms has been obtained by calcium medication. If a high guanidine level continues too long without the inhibiting action of extra calcium, irreparable tissue changes may result and in themselves cause death.

Calcium gluconate has been used exclusively in our clinical cases. In the animal experiments practically any mode of furnishing calcium ions was found effective.[5] The chief advantage of calcium gluconate is that

13. Ellsworth, R.: Guanidine Base Concentration in Blood of Normal Individuals and in Patients with Liver Injury, Bull. Johns Hopkins Hosp. **46**:296, 1930.

14. Paton, D. N., and Findlay, L.: The Parathyroids: Tetania Parathyreopriva, Its Nature, Cause and Relation to Idiopathic Tetany; The Etiology of the Condition and Its Relationship to Guanidine and Methyl Guanidine Intoxication, Quart. J. Exper. Physiol. **10**:318, 1916.

15. Cutler, J. T.: Unpublished data.

it can be injected intramuscularly without producing irritation. It can be given intravenously when desirable and any leakage around the vein will do no harm. An intramuscular depot of calcium solution furnishes a constant slow supply of calcium to the blood, which, except in urgent cases, is probably preferable to a sudden flooding of the blood stream with calcium. Even when intravenous medication is indicated at first, it is desirable to follow it with intramuscular injections of the calcium solution. In the amounts used we have seen no unfavorable reactions. Because of the dangers known to be associated with the intravenous injection of calcium salts we have always given the calcium gluconate diluted to a one per cent solution and have injected it very slowly.

SUMMARY

1. Certain very sick infants whose condition has been designated as alimentary intoxication present symptoms similar to those seen in animals suffering from guanidine poisoning.

2. Five cases of alimentary intoxication are reported in infants whose blood chemistry was similar to that found in guanidine poisoning in experimental animals.

3. Improvement followed calcium therapy in these infants just as it had been observed to follow the same treatment in animals with high guanidine levels in the blood.

THE COMPOSITION OF GROWTH

II. THE FULL-TERM INFANT *

WILLIAM W. SWANSON, M.D.
Fellow in Child Development of the National Research Council
CHICAGO

In a previous paper [1] a study was made of the mineral and nitrogen retained by a premature infant per kilogram of gain in weight. In this paper the same method of study has been carried out, with few modifications, on two normal full-term infants, one fed on cow's milk and one on breast milk. The object of this study is to determine the mineral balances over a period long enough to obtain true representative values of the several mineral and nitrogen retentions per unit of growth.

Within the last few years several interesting papers on this subject have been published, especially by Rominger and Meyer [2] and Rominger, Fasold and Meyer [3] and also by Boldt, Brahm and Andresen.[4] The balance experiments of these authors do not lend themselves entirely for comparison with those presented here, since in most of their experiments only calcium and phosphorus were determined and the more general conclusions were based on the determination of total base or of total ash. Mineral balances during longer or shorter periods have been published also by other investigators, none of them, however, covering periods long enough to afford reliable figures for the retentions of all the minerals per kilogram of gain in weight.

Two full-term healthy infants were chosen for this investigation. Their ages at the beginning and at the end of the experiment are shown in chart 1. Neither infant had any infection during the entire time of the experiment.

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* Submitted for publication, April 8, 1931.

* This investigation received financial aid from the Howland Memorial Fund.

* From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University, and the Bobs Roberts Memorial Hospital and Department of Pediatrics, the University of Chicago.

1. Hamilton, B., and Moriarty, M.: The Composition of Growth in Infancy: A Premature Infant, Am. J. Dis. Child. **37**:1169 (June) 1929.

2. Rominger, E., and Meyer, H.: Mineralstaffwechseluntersuchungen beim Säugling; die Salzretention des gesunder Brust und Flaschenkindes, Arch. f. Kinderh. **80**:195, 1927.

3. Rominger, E.; Fasold, H., and Meyer, H.: Methodik zur Durchführung langfristiger ununterbrochener Mineral- und Stickstoffwechseluntersuchungen beim Säugling, Arch. f. Kinderh. **88**:179, 1929.

4. Boldt, F.; Brahm, C., and Andresen, G.: Langfristige Mineralstoffuntersuchunger an zweigesunden Säuglingen bei mineralstoffarmer und-reicher Kost, Arch. f. Kinderh. **87**:277, 1929.

METHODS

Infant 1 was fed from a 25 pound can of whole powdered milk during the experimental period of four and one-half months. He was started on 8 Gm. of powdered milk to the hundred cubic centimeters, with the addition of 6 per cent cane sugar; later, as became necessary, the volume and strength of the powdered milk were increased. Distilled water was given freely, and on every seventh day, when off the metabolism bed, the infant received ½ ounce (19.8 cc.) of orange juice. At 3 months of age the calcium and the phosphorus of the blood were determined, roentgenograms of bones were taken, and no evidences of rickets were

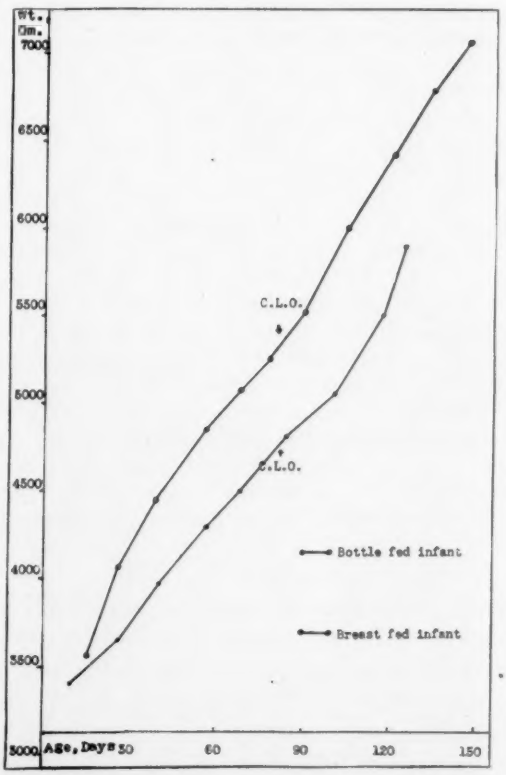


Chart 1.—Gains in weight of full-term, new-born bottle-fed and breast-fed infants before and after the administration of cod liver oil.

found. Nevertheless at this age the infant was started on cod liver oil, 1 teaspoonful twice a day, to prevent the development of rickets. This infant was started on the balance experiment when 2 weeks old and continued on the metabolism bed for consecutive six day periods with one day of rest intervening, for seventy-six days; then every other week for a second period of fifty-six days. The infant gained during the experiment 3,475 Gm., having at 5½ months more than doubled his birth weight.

Infant 2 was on a pooled supply of breast milk for 2 months, then cow's milk for one week, after which breast milk was again available for a further two month period. Distilled water, orange juice and cod liver oil were administered as in the case of infant 1. This infant was started on the metabolism bed when 10 days old and continued on the metabolism bed for six day periods with intervals of one day rest, for seventy-seven days; then every other week for another twenty-six days. He gained during the experiment 2,330 Gm., a slightly slower gain than in the case of the infant on cow's milk.

The methods used in determination of the various minerals and nitrogen may be stated briefly. Sodium was determined by adaptation of the Barber and Kolthoff method.[5] Potassium was determined by a method described by Fiske.[6] Calcium and magnesium were determined by methods suggested by Fiske. The principles of these methods may be briefly summarized. Calcium is precipitated in a slightly acid solution as oxalate. The precipitate is then collected by filtration or by centrifugation, and after ignition the calcium oxide is determined by titration with two hundredths normal hydrochloric acid. The supernatant fluid from the calcium precipitation is evaporated to dryness in a platinum dish. It is then taken up from the platinum dish in an acid solution and transferred to a test tube and the magnesium present precipitated in an alkaline solution as magnesium ammonium phosphate. The magnesium is indirectly calculated from the determined phosphorus in the magnesium salt. Chlorine was determined by the method of Laudet.[7] Phosphorus was determined by a method described by Fiske and Subbarow.[8] Sulphur was determined by a method introduced by Fiske.[9] Nitrogen was determined by the Kjeldahl method. It should be stated that the methods mentioned must be adapted to the substance used for analyses. Ashings were made at temperature ranging from 300 to 400 C. for four days. If not completely ashed at that temperature and length of time, the partially ashed material was leached with a weak acid solution and filtered. The filter paper and remaining substance was reashed, again leached, and added to the first portion. Dry ashings were found satisfactory for determination of calcium, magnesium, sodium, potassium and phosphorus, while chlorine, sulphur and nitrogen were determined separately on each specimen.

The results of this study are presented in tables 1 and 2. From these data daily retentions may readily be calculated. Some difference of opinion may arise as to the most accurate method for calculating the retentions per kilogram of gain in weight. If the infant stays on the metabolism bed almost continuously, and the days off are few, it is reasonable to assume that the days of rest would have an average daily retention approximately equal to the average daily retention of the experimental period before and after the rest period. If one does not wish to make this assumption, one can leave out the rest days and subtract the gain in weight made on these days from the total gain. However, if the gain in weight takes place at a uniform rate and retentions

5. Barber, H. H., and Kolthoff, I. M.: J. Am. Chem. Soc. **50**:1625, 1928.
6. Fiske, C. H.: J. Biol. Chem. **67**:XVI, 1926.
7. Laudet, M. M.: J. de pharm. et chim. **16**:168, 1917.
8. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.
9. Fiske, C. H.: J. Biol. Chem. **47**:59, 1921.

show small periodical fluctuations, either method of calculating the total retentions per kilogram of gain in weight is satisfactory. The retentions per kilogram of gain in weight shown in table 4 are obtained from tables 1 and 2 and are based on actual experimental days.

Table 1 shows the retentions of nitrogen and minerals per period for the infant on cow's milk. It will be seen that cod liver oil caused a slight increase in the retention of sodium, potassium and chlorine,

TABLE 1.—*Infant on Breast Milk: Total Retentions of Nitrogen and Minerals in Millimols Per Period*

Period	Number of Days	Potassium	Sodium	Calcium	Magnesium	Chlorine	Phosphorus	Sulphur	Nitrogen	Comment
1	5	9.8	15.1	1.5	1.47	11.9	3.3	2.26	181.5	.....
2	4	8.9	9.7	2.1	1.11	0.8	2.6	1.60	155.2	.....
3	7	17.4	23.2	—2.9	1.47	19.6	7.7	4.01	322.0	.....
4	6	19.2	20.3	—0.5	0.97	16.6	6.9	5.66	301.0	.....
5	6	16.4	15.2	4.4	1.95	14.4	3.8	3.54	273.0	.....
6	6	15.7	5.0	—1.0	—0.10	7.8	4.2	2.34	182.0	.....
7	5	28.1	28.6	6.3	4.17	24.4	9.9	....	431.0	Period on cow's milk
8	6	22.6	20.4	3.6	1.43	19.6	—0.4	....	246.0	.....
					After Cod Liver Oil					
9	6	16.6	16.7	0.8	2.08	8.4	2.0	2.58	249.7	.....
10	6	15.5	15.4	6.8	1.63	13.9	4.8	4.05	227.4	.....
11	6	17.6	15.5	9.3	1.70	7.0	10.2	3.50	262.0	.....
12	6	11.2	5.4	20.0	4.08	14.8	12.0	—1.83	186.0	.....
13	6	11.7	14.2	16.8	1.72	16.0	15.4	1.99	176.6	.....

TABLE 2.—*Infant on Cow's Milk: Total Retentions of Nitrogen and Minerals in Millimols Per Period*

Period	Number of Days	Potassium	Sodium	Calcium	Magnesium	Chlorine	Phosphorus	Sulphur	Nitrogen
1	5	31.0	30.3	12.2	5.5	52.9	16.0	4.43	370.2
2	6	29.6	29.1	19.5	4.3	33.3	20.2	4.55	421.0
3	6	32.6	27.2	13.3	5.4	27.3	15.0	3.38	412.5
4	6	23.6	28.4	17.7	4.7	30.0	13.6	3.63	388.0
5	6	19.3	31.5	13.6	4.7	24.9	15.9	2.35	342.5
6	6	29.9	32.9	19.0	4.4	30.8	20.1	2.48	395.7
7	6	34.1	26.0	18.7	5.5	31.8	19.4	3.27	438.0
8	6	22.3	23.6	22.8	4.0	23.7	19.3	0.55	362.0
					After Cod Liver Oil				
9	6	28.0	21.3	33.6	4.3	25.9	25.0	1.34	370.7
10	6	23.1	26.7	36.8	3.4	28.3	23.6	1.54	381.8
11	6	30.2	43.0	47.8	4.6	43.2	31.1	1.17	403.0
12	6	36.4	30.0	39.9	4.5	29.5	24.6	0.38	392.0
13	6	35.6	29.5	42.1	4.9	34.6	23.2	—2.58	374.3
14	6	32.5	41.7	61.8	0.8	57.4	33.5	—0.60	449.0

a marked increase in that of phosphorus and calcium and no change or a decrease in that of magnesium, nitrogen and sulphur.

Table 2 shows the retentions of nitrogen and minerals per period for the infant on breast milk. It will be seen that the retentions per period when compared with those of the infant on cow's milk are, except in the case of sulphur, much less. Period 7 illustrates the change that occurs in the retentions when cow's milk is introduced. There appeared to be a better mineral retention in period 8 following the period

of cow's milk, when the infant was again entirely on breast milk. Both these periods have been excluded in calculations for daily retentions and retentions per unit gain in weight.

In table 3 the daily retentions are shown for the infants on breast and cow's milk, respectively. Except for the low retentions of calcium and phosphorus in the first three months in the breast-fed infant, the values presented compare well with the table computed by Hamilton and Moriarty.[1] In spite of these low calcium and phosphorus retentions, neither an analysis of the blood nor roentgenograms of bones showed any evidence of impending rickets. No values for the retention of sulphur so far have been found in the literature, and no explanation can be offered at this time why the retention of sulphur should be greater in the infant on breast milk.

TABLE 3.—*Daily Retention of Minerals in Millimols*

Infant		Age, Mo.	Sodium	Potassium	Calcium	Magnesium	Chlorine	Phosphorus	Sulphur	Nitrogen
Before cod liver oil	Infant on breast milk	1–3	2.53	2.50	0.10	0.20	2.02	0.81	0.56	40.4
	Infant on cow's milk	1–3	4.87	4.56	2.87	0.82	4.84	2.97	0.50	66.6
After cod liver oil	Infant on breast milk	3–6	2.24	2.42	1.79	0.37	2.00	1.48	0.34	36.7
	Infant on cow's milk	3–6	5.62	5.19	7.28	0.63	6.08	4.47	0.04	65.9

TABLE 4.—*Retention of Minerals in Millimols*

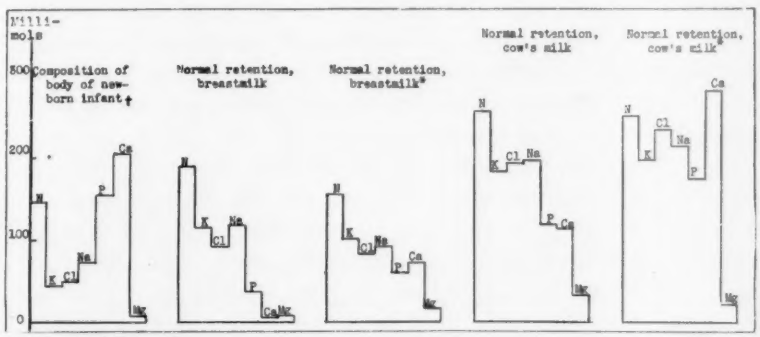
Infant		Age, Mo.	Sodium	Potassium	Calcium	Magnesium	Chlorine	Phosphorus	Sulphur	Nitrogen
Before cod liver oil	Infant on breast milk	1–3	116	114	4.7	8.97	92.3	37.2	25.4	1851
	Infant on cow's milk	1–3	196	183	117.0	32.90	194.5	119.0	20.2	2675
After cod liver oil	Infant on breast milk	3–6	93	101	74.4	15.50	84.0	61.6	14.3	1529
	Infant on cow's milk	3–6	215	197	279.0	23.90	233.0	171.0	1.3	2523

Table 4 is submitted to show the total retentions per kilogram of gain in weight. These results are obtained by dividing the retentions for a number of periods by the gain in weight as explained earlier in the paper. It may be seen that cod liver oil exerts an immediate effect on the retention of calcium and phosphorus in the two infants.

In chart 2 the absolute retentions per kilogram of gain in weight are shown and compared with the composition of the body of the full-term infant at birth. In chart 3 the same comparison is made, although in this chart the composition of the body of the full-term infant at birth is taken as 100. It is apparent that the absolute and the relative values illustrated in the two charts give entirely different impressions as to the amounts of minerals and nitrogen retained. In chart 2 all the minerals and nitrogen are presented in their true proportions as found in the composition of the body at birth, and as retentions during

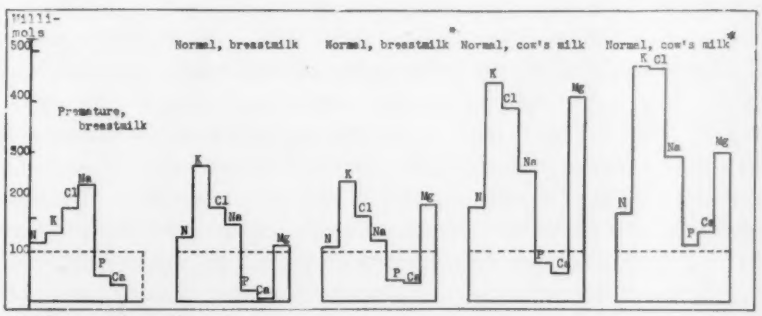
growth. The most interesting fact in this chart is the apparent equivalent distribution of potassium, chlorine and sodium in the various illustrations.

Illustration 1 in chart 3 is taken from Hamilton and Moriarty's paper [1] and is included for comparison with retentions of the full-term



* After cod liver oil.
† Cf. Hamilton and Moriarty (footnote 1, p. 1172).

Chart 2.—Retentions of minerals per kilogram of increase in body weight contrasted with the composition of the body of the new-born infant in millimols per kilogram of body weight. For convenience nitrogen represents one-tenth of the actual value.



* After cod liver oil.

Chart 3.—Diagrams drawn to same scale showing composition of 1 Kg. of growth. The composition of new-born full-term infants has been taken as 100 per cent and is indicated by the rectangle.

infant. In general, the first three illustrations show that, apparently, there is little difference in the total amount of minerals retained for each kilogram of growth in the breast milk-fed premature and the full-term infant. There is, however, a difference in the kind of minerals retained in that the full-term infant retains more potassium, but less sodium, calcium and phosphorus than the premature.

The retentions of calcium and phosphorus in the two full-term infants per kilogram of gain in weight are much less than the amounts of these minerals found per kilogram of body weight for full-term infants at birth. This appears to be a constant finding and confirms the results obtained in the previous paper [1] and also the low calcium retention shown during the first few months of life by Rominger, Fasold and Meyer.[3] It appears as if during the first months of postnatal growth the infant were using for growth some of the calcium and phosphorus present in the body at birth. In respect to magnesium it is quite the opposite in that the retentions per unit of growth exceed the concentration per unit of body weight at birth.

The difference in amounts of sodium and potassium per unit of growth in the premature breast milk-fed and the full-term breast milk-fed infant deserve a few words of comment. The increase in the concentration of sodium in the premature infant indicates either the growth of cartilage, which is very rich in sodium, or an increase in intracellular fluid and plasma. The increase of potassium in the full-term infant indicates cellular growth and the most probable growth is increase in muscle tissue. It may be possible to be more definite as to the meaning of these variations in the concentrations of the minerals and type of growth indicated when more data are available for comparison.

The last two illustrations in chart 3 show higher values for all the minerals per unit of growth in the infant fed on cow's milk and indicate an excessive mineral retention. It has been suggested by Rominger and Meyer [2] and others that this increased retention is in the form of storage in the body tissues, and that at some convenient time there is an outflow of minerals from the infant on cow's milk. During the four and one-half months of observation, as shown by table 1, there was never at any time evidence of any such outflow of minerals. Boldt and co-workers [4] have attempted to show that there is an outflow of minerals from infants fed on cow's milk when they are changed to breast milk. The evidence presented is not very convincing, since one of the infants gained on the average only 3.7 Gm. per day for twenty-six days and the other infant 14 Gm. per day for thirty-three days. It appears as though some nutritional disturbance might account for the few negative balances occurring on the first few days after breast milk was introduced.

At least two sources of probable error must be considered when speaking of supermineralization of an infant fed on cow's milk. The most important of these is the amount of mineral excretion through the skin. Probably the most important and recent paper on this subject is that by Rominger and Meyer.[10] They determined the sodium and

10. Rominger, E., and Meyer, H.: Ueber die Mineralausscheidung durch die Haut beim Säugling, Ztschr. f. Kinderh. **47**:721, 1929.

potassium chloride excreted by infants fed on cow's milk, and found that from 7 to 11 per cent of the combined retention of sodium, potassium and chloride may be excreted through the skin in the form of chlorides. As no attempt was made in this study to determine the excretion through the skin, the calculated retentions of sodium, potassium and chlorine must be from 5 to 10 per cent too high. There is, however, every reason to suppose that this error would be of about the same magnitude in the breast-fed, and bottle-fed infant.

The second source of error is the variation in storage of fat in the two infants. If the infant on cow's milk stored less fat than the infant on breast milk, it would be correct to assume that the mineral retention should be higher in the unit of growth of the infant on cow's milk. However, the infant fed on cow's milk retained per kilogram of growth approximately 80 per cent more sodium, 98 per cent more potassium and 140 per cent more chlorine. Since both infants showed a perfectly normal development, it is very improbable that the variation in fat storage would explain the differences in mineral retention per unit of growth of the two infants.

COMMENT

The data presented indicate that supermineralization takes place in an infant on a food higher in concentration of salt than that intended by nature. No definite evidence is available to show that this is detrimental to the infant. The idea, however, may suggest itself that the disturbances attributed to continued feeding of whole cow's milk may be due in part to this increased mineral retention. It appears difficult to believe that the tissues or the body fluids of the infant on cow's milk actually have a different chemical composition from that of the tissues or of the body fluids of the infant on breast milk. However, the large excess of minerals retained by the artificially fed infant must be deposited somewhere, and the location of this storage is a problem for further investigation. From the data presented it is evident that growth does not parallel the mineral retention of the artificially fed infant. Recently, Rominger, Berger and Meyer [11] have shown that the addition of sodium chloride to the food of young infants actually inhibited their growth. Meyer [12] working with rats also found that a

11. Rominger, E.; Berger, I., and Meyer, H.: Klinisch-experimentelle Untersuchungen über die Beziehungen zwischen Wasser- und Kochsalzumsatz beim gesunder Säugling, Ztschr. f. Kinderh. **48**:43, 1929.

12. Meyer, H.: Ueber Salzpeicherung bei waschsenden Tieren, München. med. Wchnschr. **74**:521, 1927.

diet high in salt (four times the normal) inhibited growth. It would appear from these investigations that a food high in minerals is not necessarily conducive to good growth.

SUMMARY

1. Retentions of minerals and nitrogen per day and per kilogram of gain in weight are reported for two normal infants, one on breast milk and one on cow's milk. The infant fed on breast milk was on the balance experiment 103 days and the infant fed on cow's milk 132 days.

2. The gain in weight per month for the breast-fed infant and the infant on cow's milk was, respectively, 700 and 770 Gm.

3. The retentions of minerals and nitrogen per unit of growth, except in the case of sulphur, were considerably higher in the infant on cow's milk. The addition of cod liver oil to the diet of the two infants increased markedly the retentions of calcium and phosphorus, but affected rather indifferently the retentions of the other materials.

Dr. B. Hamilton suggested the problem and Dr. E. A. Park provided facilities for this study.

CREATINE AND CREATININE METABOLISM IN PROGRESSIVE MUSCULAR DYSTROPHY

REPORT OF TWO CASES AND CONTROLS *

M. CATHERINE MAGEE, M.S.
Chemist, Department of Pediatrics
ANN ARBOR, MICH.

It is known that there is a change in creatine and creatinine metabolism in muscular dystrophy which causes creatinuria and decreased creatinine excretion. Why this change occurs is still open to speculation. It can be accepted that the lowered creatinine excretion is due to degeneration of the muscle fibers, for Shaffer [1] showed that the creatinine excretion is an index of muscular development. An explanation for the presence of creatinuria is more difficult. The breakdown of the muscle causing the liberation of creatine is one explanation that has been offered. This does not appear feasible because the relatively small amounts that would be liberated in the breakdown of the muscle fibers could not account for the large quantity of creatine excreted over a period of years. An explanation that appears to be more logical is that creatine is being formed at a slower rate than normal, and due to the degeneration of the muscle it is not being normally utilized. This theory is substantiated by the work of Gibson, Martin and Buell.[2] They show that the total creatinine coefficient is inversely proportional to the extent of the disease in the cases studied, that is, the more extensive the dystrophy the lower the total creatinine coefficient.

Some are of the opinion that muscular dystrophy is associated with an endocrine imbalance. Janney, Goodhart and Isaacson [3] found a hypoglycemic condition in the nine cases they studied. In five of the nine cases there was a poor utilization of dextrose. Dextrose tolerance

* Submitted for publication, April 9, 1931.

* From the Department of Pediatrics and Infectious Diseases, University Hospital, University of Michigan.

* Presented in part at the meeting of the University of Michigan Pediatrics and Infectious Disease Society, Ann Arbor, November, 1930, and the Michigan Academy of Science, Ann Arbor, March, 1931.

1. Shaffer, P. A.: Am. J. Physiol. **23**:1, 1908.

2. Gibson, R. B.; Martin, F. T., and Buell, M.: Metabolic Study of Progressive Pseudohypertrophic Muscular Dystrophy and Other Muscular Atrophies, Arch. Int. Med. **29**:83 (Jan.) 1922.

3. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: Muscular Dystrophy, Arch. Int. Med. **21**:188 (Feb.) 1918.

tests caused a higher percentage increase in blood sugar than normal, and glycosuria in a few of these cases. Roentgenograms showed rarefaction of the bones of the skull and of the long bones in eight of the cases; in two of these cases a pineal shadow was observed. Hughes and Shrivastava [4] reported two cases that showed an abnormal response to dextrose. The blood sugars during fasting were high, 160 and 170 mg. The ingestion of 50 Gm. of dextrose caused in one case hyperglycemia and glycosuria; in the other, hyperglycemia, the blood sugar rising to 240 mg. In four of the nine cases reported by Gibson, Martin and Buell,[2] hypoglycemia was observed. Kure and Okimka [5] reported improvement in cases of dystrophy on the injection of epinephrine and pilocarpine. They do not report any observations on the carbohydrate metabolism of their cases.

In this clinic two cases of muscular dystrophy were available for study.

REPORT OF CASES

CASE 1.—A white boy, aged 11 years, was admitted to the clinic on Sept. 11, 1930, with a complaint of paralysis. At the age of 4 years he did not walk, and had only begun to talk. He had been placed in a training school but became progressively weaker. He could not arise from the sitting or recumbent position. He fell over easily and had a waddling gait. The family history was unimportant.

Physical examination showed a poorly developed, mentally deficient child (moron grouping). The muscles of the lower extremities were very weak. The thigh muscles were of normal size, but the calf muscles were characteristically increased in size. The muscles of the shoulders and arms were somewhat atrophied. Biceps and triceps reflexes were questionable, and the knee jerks were negative. The abdominal reflexes were questionable.

Biopsy of the calf muscle showed fatty infiltration, atrophy and active interstitial myositis. The diagnosis was Zenker's necrosis and lipomatous pseudohypertrophic muscular dystrophy.

The basal metabolic rate was + 5 per cent. The blood, urine and other physical findings were negative.

CASE 2.—A white boy, aged 13 years, was admitted to the clinic on Nov. 12, 1930. He was fairly well nourished, and had a normal mentality. He was an adopted child, and a family history could not be obtained. The patient stated that he had had a waddling gait since infancy, but that it had become more pronounced in the past few months.

Physical examination showed marked development of the calf muscles, atrophy of the right thigh muscles, bilateral weakness of the adductors of the hips and of the abductors of the right hip. There were marked weakness of the gluteus medius and kyphosis in the lumbar region. The pectoral muscles and elevators of the scapula were slightly atrophied. There was marked weakness of the hands. When the patient arose from the sitting position with his legs crossed under him he had to "crawl up himself" in a manner characteristic of the dystrophic con-

4. Hughes, T. A., and Shrivastava, D. L.: Indian J. M. Research **15**:437, 1927.

5. Kure, K., and Okimka, S.: Klin. Wchnschr. **9**:1168, 1930.

dition. The Trendelenburg sign was positive on both sides. The knee and ankle jerks were active. There was bilateral plantar flexion and no pathologic reflexes.

Biopsy of the gastrocnemius showed an increase in interstitial nuclei, no displacement by adipose tissue, and no indications of pseudohypertrophy.

TABLE 1.—*Daily Creatine and Creatinine Excretion in Case 1*

Date	Urine Volume, Cc.	Preformed Creatinine, Mg.	Creatine as Creatinine, Mg.	Total Creatinine, Mg.	Creatinine Coefficient	Total Creatinine Coefficient	Comment
10/10/30	800	91	206	297	1.4	3.7	Diet started
10/11/30	800	123	326	449	1.8	6.7	
10/12/30	450	115	265	380	1.7	5.7	
10/13/30	1,220	134	193	327	2.0	4.9	Hourly specimens
10/14/30	1,130	150	285	435	2.3	6.6	
10/15/30	1,350	145	285	430	2.2	6.5	
10/16/30	2,105	120	293	413	1.8	6.2	Dextrose tolerance test, hourly specimens
10/18/30	900	144	236	380	2.2	5.9	
10/20/30	760	111	243	354	1.7	5.5	
10/22/30	599	134	249	383	2.1	6.0	Emesis, 8, 10, 11 a.m.
10/23/30	2,355	81	181	262	1.3	4.1	Hourly specimens
10/24/30	2,511	126	194	320	1.9	5.0	Dextrose tolerance test, hourly specimens
10/26/30	620	162	278	440	2.5	6.7	
10/27/30	1,150	117	147	264	1.8	4.2	
10/28/30	780	142	264	406	2.2	6.4	
10/29/30	2,009	144	264	408	2.2	6.4	Hourly specimens
10/30/30	1,578	124	230	354	1.9	5.4	Fasting until noon; hourly specimens
10/31/30	1,175	165	1,060	1,225	2.5	...	1 Gm. creatine orally at 8 a.m.
11/ 1/30	778	114	242	356	1.7	5.5	Hourly specimens
11/ 2/30	900	130	245	375	2.0	5.7	
11/ 3/30	900	125	228	353	1.9	5.4	
11/ 4/30	840	105	226	331	1.6	5.4	
11/ 5/30	870	150	290	440	2.3	6.7	
11/ 6/30	790	160	320	480	2.4	7.3	
11/ 7/30	515	172	443	625	2.6	9.5	Gastric upset
11/ 8/30	430	159	267	426	2.4	6.5	
11/ 9/30	480	88	254	342	1.3	5.2	
11/10/30	860	190	400	590	2.9	9.0	
11/11/30	890	158	337	495	2.4	7.5	
Minimum		81	147		1.3	3.7	
Maximum		190	443		2.9	9.5	
Average		134	274		2.0	6.0	
Variation		−39% +42%	−46% +61%				
11/12/30	930	182	117	299	2.8	4.5	High carbohydrate diet
11/13/30	720	143	187	330	2.2	5.1	
11/14/30	700	155	189	344	2.3	5.2	
11/15/30	985	129	257	386	2.0	6.0	
11/16/30	1,300	166	314	480	2.5	7.3	
11/17/30	380	184	70	250	2.8	3.8	
11/20/30	1,060	148	307	455	2.3	6.8	
11/21/30	810	142	273	415	2.3	6.2	
Minimum		129	70		2.0	3.8	
Maximum		184	314		2.8	7.3	
Average		156	214		2.4	5.6	
Variation		−17% +18%	−67% +46%				

The patient had septic and hypertrophic tonsils.

A roentgenogram of the sella turcica was negative. The basal metabolic rate was —9 per cent. The blood, urine and other physical findings were negative.

CREATINE AND CREATININE EXCRETION

The creatine and creatinine metabolism of these two patients and of two normal boys was studied. For the duration of the observation a normal, well balanced diet containing no meat or meat stock with an average daily intake of 50 Gm. of protein and from 1,600 to 1,800 calories was maintained.

The methods used were Folin-Wu [6] for blood sugar, and Folin [7] for creatinine and creatine (picric acid method). All determinations of creatine and creatinine were made on twenty-four hour specimens, the determinations being completed within the next twenty-four hours. When indicated, they were made on hourly specimens from 8 a. m. until 5 p. m., and on the pooled specimens from 5 p. m. until 7 a. m.

The creatine and creatinine excretion in case 1 was studied for forty days (chart 1). The results are tabulated in table 1. There was

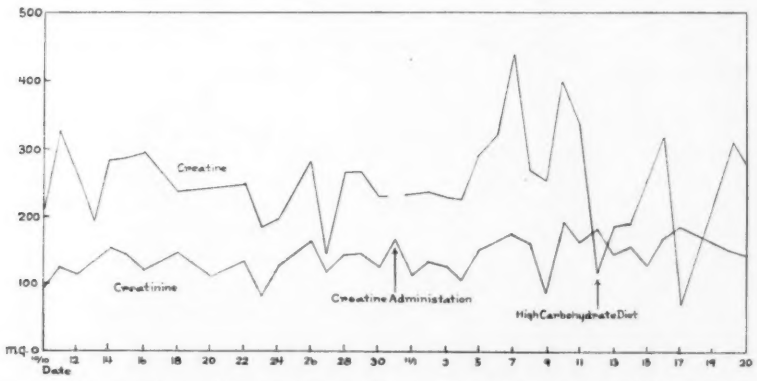


Chart 1 (case 1).—Daily excretion of creatine and creatinine.

a great variation in the daily excretion of creatinine, the average being 134 mg. with a variation of —39 and +42 per cent. All reports in the literature of creatinine excretion in muscular dystrophy have shown a marked fluctuation in the daily creatinine excretion, with the exception of the case reported by McCrudden and Sargent.[8] The fluctuation in the creatine excretion was even more marked. The average was 274 mg., with a deviation of —46 and +61 per cent. This is twice the daily excretion of creatinine. The creatinine coefficient is far below normal, an average of 2. The total creatinine coefficient is also below normal, an average of 6. Since the preformed creatinine coefficient is farther below normal than the total creatinine coefficient, this would

6. Folin and Wu: J. Biol. Chem. **41**:367, 1920.

7. Folin, O.: Biol. Chem. **17**:469, 1914.

8. McCrudden, F. H., and Sargent, C. S.: Hypoglycemia, Arch. Int. Med. **17**:465 (April) 1916.

indicate an inability of the body to convert creatine into creatinine, and some impairment in the formation of endogenous creatine. Harding and Goebler [9] showed that the total creatinine coefficient of the child should approximate the creatinine coefficient of the adult, 7-11.

TABLE 2.—*Hourly Excretion of Creatine and Creatinine in Case 1*

	Normal Day, October 29			1 Gm. Creatine Orally at 8 a.m., October 31		
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	55	5.3	12.5	51	18.0	15.3
9 a.m.	78	6.1	17.9	135	18.8	92.2
10 a.m.	270	8.5	30.0	270	9.5	200.5
11 a.m.	278	8.1	27.0	30	5.4	103.6
12 m.	260	6.3	23.0	21	6.8	79.4
1 p.m.	43	5.5	17.2	28	7.3	92.7
2 p.m.	112	9.3	25.5	24	7.3	78.7
3 p.m.	88	1.7	6.0	59	8.1	58.9
4 p.m.	335	5.9	17.9	180	7.5	46.5
5 p.m.	240	7.0	15.2	55	3.2	24.8
5 p.m.–7 a.m.	250	80.0	72.0	322	73.0	267.3
Total	2,009	143.7	264.2	1,340	164.9	1,059.9

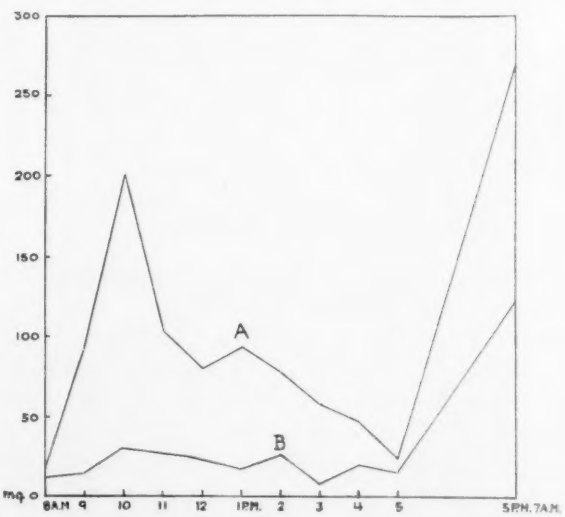


Chart 2 (case 1).—*A*, hourly excretion of creatine after the ingestion of 1 Gm. at 8 a. m.; *B*, hourly excretion of creatine on a normal day.

The changes in the hourly excretion of creatine due to the ingestion of 1 Gm. of this substance are given in table 2. The maximum excretion (10 a. m.) of the exogenous creatine occurs two hours after its ingestion (chart 2). This excretion drops rapidly during the day until

9. Harding, V. J., and Goebler, O. H.: J. Biol. Chem. **54**:579, 1922.

it is almost at the normal level at 5 p. m. There was a continued excretion throughout the night, 264 mg. being excreted, while during a normal night only 72 mg. was excreted. Forty per cent of the exogenous creatine was recovered in five hours, 60 per cent in nine hours and 80 per cent in twenty-four hours. There was no increase in creatinine on the day of creatine administration, nor was there any increased creatine or creatinine excretion on the following day.

It is interesting to note that on November 7 there was a decided gastric disturbance coincident with the largest amount of creatine (443 mg.) excreted during the experiment. The urine was free from diacetic acid.

In this case the blood sugar during fasting was normal for a child, 83 mg. Table 3 shows a normal dextrose tolerance curve after the

TABLE 3.—*Dextrose Tolerance Test* *

	Case 1		Case 2			
					Dec. 12, 0.5 Cc. of 0.1% Epinephrine Subcutaneously and Dextrose Orally	
Time	Oct. 16, Blood Sugar, Mg. per 100 Cc.	Oct. 24, Blood Sugar, Mg. per 100 Cc.	Dec. 5, Blood Sugar, Mg. per 100 Cc.	Dec. 8, Blood Sugar, Mg. per 100 Cc.	Blood Sugar, Mg. per 100 Cc.	Urine Sugar, Mg. per 100 Cc.
Fasting	83	80	93	100	100	...
½ hour after dextrose ingestion	133	127	98	120	203	...
1 hour after dextrose ingestion	117	93	111	105	266	600
2 hours after dextrose ingestion	79	93	95	...	138	480
3 hours after dextrose ingestion	89	70	105	...	70	...
4 hours after dextrose ingestion	95	76	100	...	...	...

* 1.75 Gm. of dextrose per kilogram of body weight.

ingestion of 42 Gm. of dextrose (1.75 Gm. per kilogram of body weight), thus indicating a normal carbohydrate metabolism.

On November 12, the patient was put on a high carbohydrate diet, the average daily intake being 400 to 500 Gm. No meat or meat stock was allowed. The daily caloric intake was from 2,500 to 3,000 calories.

In this period of the high carbohydrate diet the creatine excretion was lower than the creatinine on two days, November 12 and 17. This never occurred in the thirty-one days previous to the change in diet. The average creatine excretion, 214 mg., was also lower during this period. Although the creatinine is apparently higher, 156 mg., it can be seen that the rise occurred previous to the initiation of the high carbohydrate diet. The average creatinine excretion for the interval of November 6 to 11 is 154 mg., for the period of the carbohydrate diet, November 12 to 21, 156 mg.

The high carbohydrate diet was given for too short a time from which to draw definite conclusions. It appears, however, that this diet had some influence on the retention of creatine.

A similar study was made on case 2. Table 4 is a summary of the daily creatine and creatinine excretion for a period of twenty-eight days.

TABLE 4.—*Creatine and Creatinine Excretion in Case 2*

Date	Urine Volume, Cc.	Preformed Creatinine, Mg.	Creatine as Creatinine, Mg.	Total Creatinine, Mg.	Creatinine Coefficient	Total Creatinine Coefficient	Comment
11/30/30	980	478	177	655	5.8	7.9	Standard diet from 11/16/30
12/ 1/30	1,310	475	150	625	5.7	7.5	
12/ 2/30	1,690	510	153	663	6.1	8.0	
12/ 3/30	1,180	483	173	656	5.8	7.9	
12/ 4/30	3,240	508	190	698	6.1	8.4	Hourly specimens
12/ 5/30	2,614	492	100	592	5.9	7.1	Dextrose tolerance test
12/ 6/30	2,163	479	588	1,067	5.8	...	1 Gm. creatine orally at 9 a.m.
12/ 8/30	3,383	577	108	685	6.9	8.2	Dextrose tolerance test
12/ 9/30	1,510	505	50	555	6.1	6.7	
12/10/30	1,080	432	83	515	5.2	6.2	
12/11/30	1,070	470	115	585	5.6	7.0	
12/12-13/30	3,032	990	73	1,063	...	...	12/12, 0.5 cc. of 0.1% epinephrine subcutaneously; 12/13, dextrose tolerance test
12/14/30	890	495	0	495	5.9	5.9	
12/15/30	1,385	466	27	493	5.7	6.0	
12/16/30	1,370	610	25	635	7.4	7.7	
12/17/30	1,270	487	27	514	5.8	6.2	
12/18/30	1,920	591	0	591	7.1	7.1	
12/20/30	2,370	534	0	534	6.3	6.3	
12/21/30	985	394	0	394	4.7	4.7	
12/22/30	1,200	487	86	573	5.7	6.7	
12/23/30	1,730	462	86	548	5.4	6.5	
12/25/30	1,175	467	58	525	5.5	6.2	
12/26/30	2,458	514	73	587	6.0	7.1	Hourly specimens
12/28/30	2,473	413	88	501	4.9	5.9	Fasting till 12 m.; hourly specimens
Minimum		394	0		4.7	4.7	
Maximum		610	190		7.4	8.4	
Average		513	...		5.9	7.1	
Variation		+19% −21%					

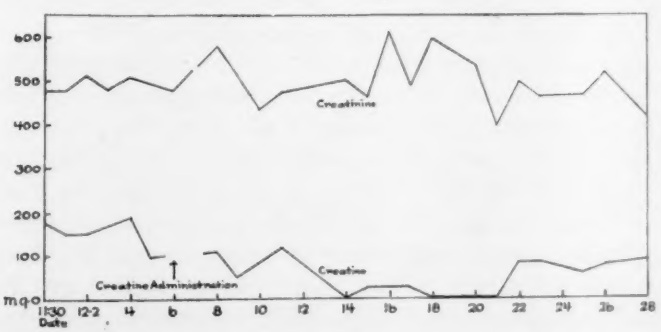


Chart 3 (case 2).—Daily excretion of creatine and creatinine.

In comparison with case 1 it was characterized by a more normal creatinine and a lower creatine excretion. During the observed period (chart 3) the creatine disappeared from the urine and then appeared

again, increasing to approximately half of the amount excreted at the beginning of the study. During the first seven days of observation, the creatinine was quite constant (±4 per cent), but as the creatine excretion became less there was a greater variation in the amount of creatinine eliminated (±20 per cent). This variation was never as marked as in case 1, which showed an extreme muscular dystrophy. The creatine excretion was less than the creatinine, but it was more than would be expected in a normal boy of this age. In normal children, the creatinurea gradually disappears as puberty is approached (cases 4 and 5). After the first six days of observation there is a diminution in creatine elimination with an increase toward the previous level in the last five days (December 22 to 27). I have been unable to explain these changes in creatine excretion. It cannot be said that exogenous creatine

TABLE 5.—*Hourly Excretion of Creatine and Creatinine in Case 2*

	Normal Day, December 4			1 Gm. Creatine Orally at 9 a.m., December 6		
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	87	58.0	16.0	...	....	....
9 a.m.	48	23.9	24.8	165	73.0	18.5
10 a.m.	405	27.7	29.7	75	29.0	96.0
11 a.m.	205	25.6	22.7	273	27.2	126.8
12 m.	252	22.0	16.7	175	26.5	89.5
1 p.m.	98	23.0	17.2	210	25.7	66.8
2 p.m.	363	24.8	18.2	80	16.3	55.7
3 p.m.	285	24.8	10.8	175	25.0	52.6
4 p.m.	340	23.2	6.3	155	24.8	43.2
5 p.m.	252	21.0	7.9	230	24.2	19.6
5 p.m.–7 a.m.	905	234.4	21.2	625	207.5	19.3
Total	3,240	508.0	191.5	2,163	479.2	588.0

stimulated the metabolism of this substance, for the creatine excretion was 100 mg. on the day previous to the administration of 1 Gm. of creatine orally (December 6) and 108 mg. the second day thereafter. The diminution in the creatine excretion is very interesting. The clinical picture improved during this period of lowered creatine excretion. The patient was able to arise from a sitting position with his legs crossed without the use of his hands. While on admission, in order to do this, he had to "crawl up himself." If the lowered creatine excretion indicates an improvement in muscular metabolism, there should have been an increase in the creatinine excretion. Shaffer showed that the creatinine coefficient is an index to muscular development. There was no increase in creatinine. On only two days (December 16 and 18) was the creatinine excretion more than in the period of high creatine elimination. One might consider that the muscle was retaining more creatine, and for this reason a lowered excretion occurred. The only explanation I have for the clinical improvement is the rest and the nourishment from a

well balanced diet while in the hospital. On December 22, there was a marked increase in the creatine excretion. It remained at this level for five days. Whether the creatine returned to the previous higher level (150 mg.) is not known for the patient left the clinic at this time.

The average preformed creatinine coefficient was 5.9. This is practically normal. It indicates a mild dystrophic condition.

The recovery in the urine of exogenous creatine (1 Gm. orally at 8 a. m. on December 6) is shown in table 5. The same rapid maximum excretion (chart 4) occurred at the second hour after the ingestion of the creatine as in case 1. The excretion of the exogenous creatine fell until it was practically normal at 5 p. m. From 5 p. m. to 7 a. m., it was less than on the normal day. There was approximately 45 per cent recovery of the exogenous creatine in eight hours. On the second day after the administration of creatine (December 8) there was an increased excretion of creatinine, 577 mg., 88 mg. more than the average

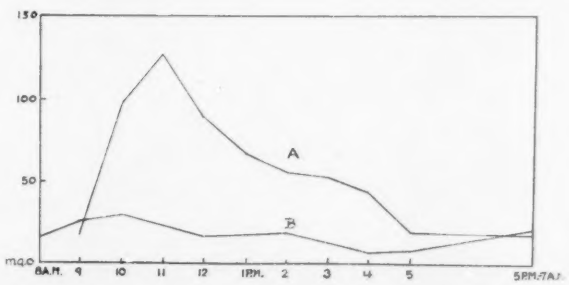


Chart 4 (case 2).—*A*, hourly excretion of creatine after the ingestion of 1 Gm. at 9 a. m., *B*, hourly excretion of creatine on a normal day.

amount in the seven previous days. On the following days the creatinine was within the normal limits of the preadministration period and remained quite constant for another seven days. It appears that 10 per cent of the exogenous creatine was converted into creatinine. Unfortunately, the specimen for December 7 was lost, so it is not known if there was an increase in creatinine on the first day following the administration of the creatine. Assuming that the excess creatinine of December 8 had this exogenous source, the total recovery of creatine was 55 per cent. Although a greater retention of creatine would be expected in a 13 year old child, this value could not be considered abnormal because of the individual fluctuation in creatine retention observed in children (cases 4 and 5).

The carbohydrate metabolism in this case, as indicated by dextrose tolerance tests (table 3), differs from those observed by Janney, Goodhart and Isaacson or by Hughes and Shrivatava. In their cases there was an inability to utilize dextrose when it was given in large

amounts. The blood sugar during fasting was normal in case 2, but it rose only 20 per cent on the ingestion of 1.75 Gm. of dextrose per kilogram of body weight. This indicates an extremely rapid utilization of carbohydrate.

The action of epinephrine (December 12) indicates a normal storage of liver glycogen. The injection of 0.5 cc. of a 0.1 per cent solution coincident with the oral administration of dextrose caused a 160 per cent increase in blood sugar and a glycosuria.

A roentgenogram of the sella turcica was negative, and there were no clinical manifestations of hypopituitarism. The basal metabolic rate was also normal.

The creatine and creatinine metabolism of two normal boys was compared with that found in the cases of muscular dystrophy. Case 4

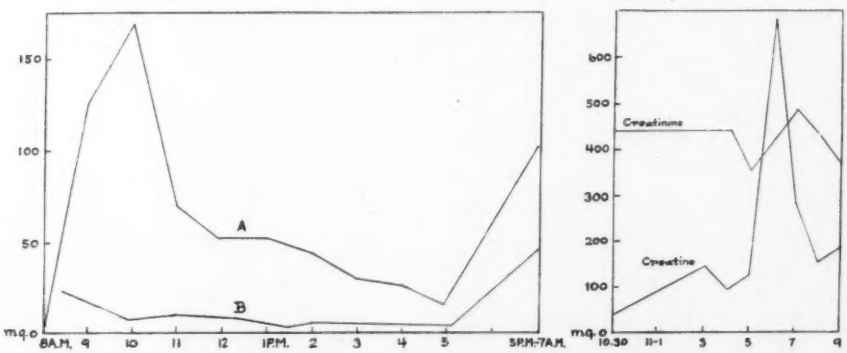


Chart 5 (case 5).—In the chart on the left *A* shows the hourly excretion of creatine after the ingestion of 1 Gm. at 8 a. m., and *B*, the hourly excretion of creatine on a normal day. The chart on the right shows the daily excretion of creatine and creatinine.

is that of a white boy 9 years of age, and case 5, of a white boy 6 years of age.

The daily creatine and creatinine excretion for short periods are given in tables 6 and 7. Case 4 shows a remarkably constant excretion of creatinine. The average is 536 mg. with a variation of ±3 per cent. The variation in the excretion in the younger child, case 5, is greater, an average excretion of 414 mg., +7 and —17 per cent (chart 5). The creatinine coefficients in these two cases are normal, 6.5 for case 4 and 7.5 for case 5. It is interesting that the higher creatinine coefficient occurred in the younger child. As would be expected, this child (case 5) had a higher creatine excretion (40 to 140 mg.) than case 4 (10 to 55 mg.). The total creatinine coefficient was above 7 in both cases, 7.1 for case 4 and 8.8 for case 5. Harding and Goebler

showed that the total creatinine coefficient of the child should equal the creatinine coefficient of the adult, 7 : 11.

The excretion of exogenous creatine (1 Gm. orally) in case 4 was 33 per cent. It is impossible to tell when the maximum excretion of exogenous creatine occurred, for the 8, 9 and 10 a. m. specimens were received as one for 10 a. m. From table 6 it can be seen that the excretion of exogenous creatine dropped rapidly throughout the day. The creatine reached the normal level at 5 p. m. and remained so through the

TABLE 6.—*Excretion of Creatine and Creatinine in Case 4, Normal Child of Nine Years*

Date	Urine Volume, Cc.	Preformed Creatinine, Mg.	Creatine as Creatinine, Mg.	Total Creatinine, Mg.	Creatinine Coefficient	Total Creatinine Coefficient
			Daily Excretion			
11/ 5/30	1,030	520	10	530	6.5	6.6
11/ 6/30	1,120	530	45	575	6.6	7.2
11/ 7/30	970	545	48	593	6.8	7.4
11/ 8/30	950	540	55	595	6.8	7.4
11/ 9/30	1,000	550	50	600	6.9	7.5
11/10/30	2,415	535	37	572	6.6	7.2
11/11/30*	3,955	612	324	936	...	...

	Hourly Excretion					
	Normal Day, November 10			1 Gm. Creatine Orally at 8 a.m., November 11		
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
8 a.m.	75	80.0	2.0	...	....	....
9 a.m.	180	28.0	2.2	...	....	....
10 a.m.	200	14.3	0	430	110.0	180.0
11 a.m.	420	42.0	3.0	290	27.0	48.0
12 m.	...	....	....	425	23.5	23.5
1 p.m.	175	30.4	3.2	420	20.0	21.0
2 p.m.	240	38.4	2.2	410	22.2	15.1
3 p.m.	140	28.0	5.0	210	23.3	10.3
4 p.m.	245	22.2	2.0	155	51.8	7.7
5 p.m.	250	16.5	0	225	11.3	1.5
6 p.m.	330	40.4	4.9	490	23.1	4.1
7 p.m.-7 a.m.	260	195.0	13.0	900	300.0	13.0
Total	2,415	535.2	37.5	3,955	612.2	324.2

* 1 Gm. creatine orally.

night. The exogenous creatine recovered from this source was 27 per cent. Six per cent appears to have been converted into creatinine. For six preceding days the creatinine was remarkably constant, but rose to 612 mg. on this day, 62 mg. above the highest amount previously excreted (550 mg.).

The recovery of exogenous creatine (1 Gm. orally at 8 a. m., November 6) in case 5 was 75 per cent (chart 5). All of this did not appear as creatine in twenty-four hours. Some exogenous creatine apparently was excreted in the second twenty-four hours after ingestion as creatine and creatinine. After the ingestion of the creatine the same maximum excretion occurs within two hours (table 7) as observed in

cases 1 and 2. The exogenous creatine dropped rapidly throughout the day but continued during the night and also during the second day. On November 7 the creatine was 283 mg., 140 mg. higher than that observed in the preadministration period. On November 8 and 9, also, the excretion was slightly greater than normal, which may have been from an exogenous source. A slight amount of the exogenous creatine (40 mg.) appears to have been converted into creatinine on the first day (November 7) after the administration of the creatine. Although the total elimination in this case was almost as great as in case 1, the rapidity

TABLE 7.—*Excretion of Creatine and Creatinine in Case 5, Normal Child of Six Years*

Date	Urine Volume, Cc.	Preformed Creatinine, Mg.	Creatine as Creatinine, Mg.	Total Creatinine, Mg.	Creatinine Coefficient	Total Creatinine Coefficient
			Daily Excretion			
10/30/30	1,820	440	40	480	7.4	8.1
11/ 3/30	1,600	440	140	580	7.4	9.8
11/ 4/30	985	444	96	540	7.4	9.3
11/ 5/30	3,547	355	128	483	6.0	8.2
11/ 6/30*	2,650	416	683	999	...	...
11/ 7/30	2,300	483	283	766	...	...
11/ 8/30	2,660	434	156	590	7.3	9.9
11/ 9/30	2,650	367	183	550	6.2	9.3

	Hourly Excretion					
	Normal Day, November 5			1 Gm. Creatine Orally at 8 a.m., November 6		
Time	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.	Urine Volume, Cc.	Creatinine, Mg.	Creatine as Creatinine, Mg.
7 a.m.	...	....	....	335	52.0	0
8 a.m.	91	36.0	23.0	46	15.3	3.1
9 a.m.	125	11.2	7.8	70	21.0	125.0
10 a.m.	520	20.6	10.0	270	17.4	162.6
11 a.m.	440	17.6	8.2	175	17.5	70.3
12 m.	370	13.4	7.9	...	....	....
1 p.m.	136	7.4	3.5	347	32.0	104.0
2 p.m.	66	20.6	5.4	100	21.0	44.8
3 p.m.	135	13.4	5.9	35	17.5	29.1
4 p.m.	99	14.2	5.6	220	14.6	25.9
5 p.m.	150	7.2	4.9	390	19.5	15.9
5 p.m.–7 a.m.	1,315	193.5	46.0	662	188.5	102.5
Total	3,547	355.1	128.1	2,650	416.3	683.2

* 1 Gm. creatine orally.

of excretion varied in the two cases. In the case of severe muscular dystrophy (case 1) the exogenous creatine was excreted only during the first twenty-four hours, while in the normal case it was excreted as creatine for forty-eight hours, and there was an increase in creatinine.

SUMMARY

The creatine and creatinine metabolism in two cases of muscular dystrophy and two normal cases has been studied.

Case 1 (extreme muscular dystrophy) showed a marked impairment in creatine and creatinine metabolism. The creatine elimination was

twice that of the creatinine. The average creatinine coefficient was 2, indicating an inability to convert creatine into creatinine. The total creatinine coefficient was also low, 6. Eighty per cent of the exogenous creatine was recovered from the urine in twenty-four hours. The dextrose tolerance curve was normal. On a high carbohydrate diet there was some diminution in the creatine excretion.

Case 2 (a mild dystrophic condition) showed a creatine and creatinine excretion at the lower level of normal. The creatinine coefficient was 5.9, and the total creatinine coefficient was 7.1. This case was characterized by a gradual reduction in creatine until there was no elimination of this substance for a few days and a reappearance of it on the last days of observation. There was no increase in creatinine excretion during this time, but there was some clinical improvement. Fifty-five per cent of the exogenous creatine was recovered in the urine, 45 per cent as creatine in eight hours and 10 per cent which apparently had been converted to creatinine on the second day after the ingestion of the creatine. This patient showed a rapid utilization of dextrose, only a 20 per cent rise after the ingestion of 1.75 Gm. of dextrose per kilogram of body weight. The blood sugar during fasting was normal, and there was no indication of hypopituitarism.

In case 4, that of a normal child 9 years of age, 33 per cent of the exogenous creatine was recovered. Twenty-seven per cent was recovered as creatine in eight hours, and 6 per cent was apparently changed to creatinine on the day of administration.

In case 5, the patient, 6 years of age, eliminated 75 per cent of the exogenous creatine. Although the total elimination in this case was almost as great as in case 1, the rapidity of the elimination was different. Exogenous creatine was excreted as creatine for forty-eight hours after ingestion, and in the second twenty-four hours there appears to have been some conversion into creatinine.

THE TRYPTOPHAN TEST IN TUBERCULOUS MENINGITIS *

HENRY H. LICHTENBERG, M.D.
CHICAGO

During the last decade a number of investigators have employed various tests in the study of spinal fluids, principally qualitative chemical reactions for the presence of tryptophan groups, with a view toward the development of methods of differential diagnosis. The literature in regard to these tests is scant and deals more, perhaps, with the results on syphilitic rather than tuberculous spinal fluids.

Brugi [1] applied the Furth and Nobel [2] modification of the Voisinet test for tryptophan to forty-two spinal fluids from patients with the following diseases: tuberculous meningitis, proved by autopsy, twelve; meningism, two; syphilis, four; uremia, two; multiple sclerosis, one; hydrocephalus, five, and five fluids were from normal persons. Only the tuberculous fluids gave a positive reaction. Aiello [3] reviewed the literature, principally Italian, and concluded that the reaction is positive in about 90 per cent of cases of tuberculous meningitis; that a negative reaction generally excludes the presence of a specific meningitis, and that there are about 2 per cent false positive reactions. The positive reaction seemed independent of the albumin and globulin content of the fluid.

METHOD

The test is a color reaction said to be given by the tryptophan groups, either free or combined. The required reagents are: (1) concentrated hydrochloric acid, (2) 2 per cent formaldehyde, made by a 1:20 dilution of the ordinary 40 per cent formaldehyde and (3) 0.06 per cent sodium nitrite. Ordinary large test tubes with a capacity of about 30 cc. and about 15 mm. in diameter are used.

To 2 or 3 cc. of spinal fluid, from 15 to 18 cc. of concentrated hydrochloric acid and 2 or 3 drops of formaldehyde are added, shaken and allowed to stand from four to five minutes. The solution is then layered with about 1 or 2 cc. of the sodium nitrite solution and allowed to stand from two to three minutes. At the junction of the two liquids a delicate violet ring is formed if the reaction is

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* Submitted for publication, April 8, 1931.

* From the Department of Pediatrics, Johns Hopkins University and the Harriet Lane Home, Johns Hopkins Hospital, Baltimore.

1. Brugi, A.: La reazione del triptofano nel liquor, Pensiero med. **12**:583, 1923.

2. Furth, O., and Nobel, E.: Colorimetrische Untersuchungen über das Tryptophan, Biochem. Ztschr. **109**:103, 1920.

3. Aiello, G.: La reazione del triptophano nel liquido cefalorachidino, Riforma med. **43**:35, 1927.

positive, and a brown ring or no ring if it is negative. The reaction is best read by daylight. The color is definite, though at times faint. In doubtful reactions the test should be considered negative. The test is roughly quantitative, so that in cases of advanced tuberculosis, 1 cc. or even 0.25 cc. will give a distinct reaction. In doubtful cases, however, it is advisable to use the full 2 to 3 cc. of spinal fluid.

RESULTS

The present communication is a report of the results obtained with this test in the spinal fluids of seventy-eight children treated at the Harriet Lane Home from May, 1929, to June, 1930. The children

TABLE 1.—*Positive Spinal Fluid Tryptophan Tests in Cases Proved to Be Tuberculous Meningitis*

Case	History No.	Age	Sex	Diagnosis on Admission	Spinal Fluid				Mantoux Tuberculin Test
					No. Cells	Mononuclear Cells	Pandy	Tubercle Bacilli	
1	67043	5 yr.	F	Tuberculous meningitis	83	88%	+	+++	—
2	64656	6 mo.	M	Tuberculous meningitis	72	90%	?	—	+
3	55801	4 yr.	M	Tuberculous meningitis	140	Chiefly	+	—	+
4	65836	2½ yr.	M	Tuberculous meningitis	128	80%	+	—	+
5	64720	2 yr.	F	Tuberculous meningitis	68	Chiefly	+	—	+
6	.....	1 yr.	F	Tuberculous meningitis	100	Chiefly	+	+++	Died before completion of test
7	64651	9 yr.	M	Tuberculous meningitis	34	80%	+	—	+
8	60207	8 mo.	F	Tuberculous meningitis	220	Chiefly	+	+	+
9	62584	1 yr.	F	Tuberculous meningitis	110	92%	+	—	+
10	34291	12 yr.	M	Tuberculous meningitis	94	85%	Slight	+	+
11	62918	4 yr.	M	Tuberculous meningitis	412	70%	+	—	+
12	62997	21 mo.	F	Tuberculous meningitis	120	89%	+	—	Not read
13	61177	9 mo.	M	Tuberculous meningitis	120	89%	+	+	+
14	63259	14 mo.	M	Cerebral hemorrhage or brain tumor or encephalitis or tuberculous meningitis	410	90%	+	—	Died before completion of test
15	66244	3½ yr.	M	Tuberculous meningitis	307	20%	+	+	+
16	59158	21 mo.	M	Tuberculous meningitis	297	80%	+	—	+
17	64568	2½ yr.	M	Tuberculous meningitis	116	72%	+	+	+
18	.....	2½ yr.	M	Encephalitis or brain abscess or tuberculous meningitis	125	66%	+	—	+
19	65274	2 yr.	F	Tuberculous meningitis or encephalitis	88	70%	+	—	+
20	65250	2 yr.	F	Tuberculous meningitis	105	90%	+	—	+
21*	60282	1 yr.	M	Tuberculous meningitis	200	90% (?)	+	—	+
22	64282	6 mo.	F	Tuberculous meningitis	100	Chiefly	+	—	+
23	39147	6 yr.	F	Tuberculous meningitis	195	90%	+	—	+
24	65543	11 mo.	F	Tuberculous meningitis	165	26%	+	+	+
25	62954	2 yr.	F	Tuberculous meningitis	211	72%	+	—	+

* Cases 20 and 21 ran typical courses of tuberculous meningitis. Both patients succumbed to the disease, but autopsies were refused and tubercle bacilli were never demonstrated in the spinal fluids.

suffered from various diseases, including tuberculous meningitis. The fluids were removed by lumbar, cisternal or ventricular puncture, and the test applied from a few minutes to several days after removal. To ascertain the specificity of the test, the following conditions which might interfere with the test were investigated. The reaction is given by whole spinal fluids and by fluids from which a sediment or a pellicle is removed. Age and bacterial contamination do not affect the reaction. Blood-tinged fluids with not more than 400 erythrocytes per cubic

millimeter do not invalidate the test, but those containing an abundance of blood give a positive reaction. The positive reaction in such fluids is due to the presence of blood serum.

The seventy-eight cases in which the tests were made have been subdivided for purposes of analysis. In table 1 are listed twenty-five cases in which a positive reaction was obtained on the first examination.

TABLE 2.—*Negative Tryptophan Tests in Abnormal Spinal Fluids in Conditions Other Than Tuberculous Meningitis*

Case	History No.	Age	Sex	Diagnosis on Admission	Spinal Fluid				Mantoux Tuberculin Test	Final Diagnosis and Comment
					No. Cells	Mononuclear Cells	Pandy	Film		
1	64199	5 yr.	F	Miliary tuberculosis, tuberculous meningitis	21	Most	Trace	0	0	Pertussis encephalitis; discharged well 5 wk. after admission
2	59418	4 yr.	M	Tuberculous meningitis	140	90%	+	0	0	Encephalitis; well after 3 weeks
3	63288	9 yr.	M	Polio-encephalitis or tuberculous meningitis	196	85%	0	0	0	Encephalitis (?); complete clinical recovery
4	63570	5 yr.	M	Polio-encephalitis, tuberculous meningitis or brain abscess	640	63%	+	0	0	Encephalitis; recovery in 17 days
5	39192	8 yr.	F	Tuberculous meningitis	760	All	±	0	0	Encephalitis; complete recovery
6	.....	16 yr.	F	Encephalitis, brain abscess or tuberculous meningitis	115	95%	+	0	0	Abscess of brain; proved at autopsy
7	58566	8 yr.	F	Lead encephalitis	14	71%	+	0	0	Lead encephalitis; mind permanently damaged; physically well
8	67118	6 yr.	M	Tetanus	3	All	+	0	0	Complete recovery
9	67178	21 mo.	F	Tuberculous meningitis	3	All	+	0	0	Cerebellar tumor; confirmed at autopsy
10	40475	6 yr.	F	Meningococcus meningitis	30	20%	Not done	0	0	Meningococcus meningitis; confirmed by autopsy
11	66462	3 yr.	F	Meningitis	14	100%	Not done	0	0	Influenza meningitis; B. influenza cultured from spinal fluid; treated with influenza serum; complete recovery

Twenty-three of these were subsequently proved to be tuberculous meningitis either by autopsy, by guinea-pig inoculation or by finding tubercle bacilli in the spinal fluid. In the remaining two, cases 20 and 21, tubercle bacilli were never demonstrated in the spinal fluid, and autopsy was refused. Clinically, however, both ran a course typical of tuberculous meningitis, and death occurred in both. The remaining thirteen cases are not tabulated, but are referred to later. In these the spinal fluids were either xanthochromic or purulent and gave false positive reactions.

The forty cases that gave a negative reaction have been subdivided into three groups. In table 2 are listed eleven cases, grouped together because of the presence of abnormal globulin content or of an elevated

TABLE 3.—*Negative Spinal Fluid Tryptophan Tests in Cases in Which Tuberculous Meningitis Is Suspected*

Case	H.L.H. No.	Age	Sex	Spinal Fluid: No. Cells	Spinal Fluid: Mononuclears	Spinal Fluid: Pandy	Diagnosis and Comment
1	65225	6 yr.	F	3	—	0	Pulmonary tuberculosis; tuberculous lymphadenitis; discharged to sanatorium
2	31014	8 yr.	F	Not increased	—	0	Autopsy; miliary tuberculosis; tuberculous peritonitis; no meningitis
3	38304	6 yr.	M	11	All	0	Pneumococcus pneumonia; well in 4 weeks
4	63408	6 yr.	M	Not increased	—	0	Tuberculosis of mediastinal lymph nodes; transferred to sanatorium
5	66956	3 yr.	M	3	All	0	Arthritis of spine; taken home against advice
6	65488	8 mo.	F	6	—	0	Pulmonary tuberculosis; left hospital unimproved

TABLE 4.—*Negative Tryptophan Tests in Conditions Other Than Tuberculous Meningitis in Which the Spinal Fluid Proved Normal* *

Case	History No.	Age	Sex	Outcome and Comment
1	66420	2 yr.	F	Appendicitis with peritonitis; autopsy: brain and meninges normal
2	65708	2 mo.	F	Pneumonia; complete recovery
3	64067	5 mo.	M	Ulcerative colitis, proved by autopsy
4	65856	11 mo.	M	Paratyphoid fever; complete recovery
5	63413	10 mo.	M	Pneumonia; complete recovery
6	66101	3 mo.	M	Staphylococcus septicemia; complete recovery
7	63193	8 mo.	M	Autopsy: pneumonia
8	61448	1 yr.	M	Autopsy: bronchopneumonia
9	64186	4 mo.	F	Autopsy: lobar pneumonia; retropharyngeal abscess
10	65649	7 mo.	M	Probably congenital cerebral defect; discharged after some weeks in hospital
11	66409	9 yr.	M	Pneumonia; complete recovery
12	65971	7 yr.	F	Bronchitis; complete recovery
13	67087	6 yr.	F	Autopsy: lobar pneumonia
14	65401	18 mo.	F	Pharyngitis; convulsions; complete recovery
15	.....	Infant	M	Autopsy: no meningeal pathologic process
16	.....	Infant	M	Discharged after several weeks
17	.....	Infant	M	Remained well
18	57081	2 yr.	M	Autopsy: bronchopneumonia; bronchiectasis
19	63810	16 mo.	F	Autopsy: dysentery; ulcerative colitis
20	64578	2 mo.	F	Autopsy: congenital syphilis
21	60478	13 days	F	Autopsy: icterus neonatorum
22	63243	3 mo.	M	Autopsy: ulcerative colitis
23	67133	8 yr.	M	Died in diabetic coma soon after admission; autopsy: peribronchial and peritracheal tuberculosis; few tubercles in lungs and spleen

* Because of symptoms that suggested intracranial inflammation, lumbar punctures were done either on admission or during stay in hospital.

cell count in the spinal fluid, or because the clinical appearance or history of the case made one suspect the possibility of a tuberculous infection of the meninges. In table 3 are listed six cases of active tuberculosis in which the spinal fluids were examined because some development in the course of the disease such as stiffness of the neck, severe

vomiting or stupor led us to suspect or wish to rule out tuberculous meningitis. Table 4 shows the results of the test in twenty-three cases with normal spinal fluids. Some of the fluids in these cases showing a meningeal involvement clinically [4] were removed shortly after death, and other fluids in this group were from patients in whom signs of meningeal irritation (meningism) developed in the course of an acute infection. These fluids showed no increase in cells or protein content and gave a negative tryptophan reaction. Those patients in table 4 who died and on whom autopsy was performed (seventeen cases) showed no evidence of tuberculous meningitis. Of those who recovered, some were followed in the outpatient department.

This study was begun with a critical attitude to ascertain by analysis of the results the practicability and reliability of the test as an aid in the differential diagnosis of tuberculous meningitis. In no instance did the diagnosis influence the reading of the test. On the contrary, the results of the test frequently influenced the diagnosis. The following cases are cited as examples of the diagnostic aid of the test in the differential diagnosis of tuberculous meningitis.

REPORT OF CASES

CASE 1 (case 14, table 1).—C. W., a 14 months old white boy, whose past history was unimportant save for whooping cough at 5 months and mastoiditis with mastoidectomy at 10 months, was well until four days before admission, when his mother noticed that he was unusually fretful. A local physician thought the child might be teething, since he found nothing else to account for the symptoms. Three days later, the child's left side twitched for ten minutes, and on the morning of admission there occurred a generalized convulsion and stiffness of the left side. On admission, the child was comatose and appeared acutely ill. The temperature was 104 F., and the respirations were irregular. The left side was rigid; the reflexes were hyperactive, and a bilateral Babinski sign was present Cerebral hemorrhage, abscess, tumor and encephalitis were considered, although tuberculous meningitis was thought to be the most likely diagnosis. The spinal fluid was under increased pressure; there were 410 cells, of which 80 per cent were mononuclears, and the Pandy reaction was positive. The tryptophan test was positive. Death occurred in a few hours. Necropsy showed healing tuberculous lesions of the lungs and mediastinal lymph nodes, miliary tubercles in the liver, spleen and kidneys and a very acute tuberculous meningitis.

CASE 2 (case 18, table 1).—L. L., a white boy, 2½ years old, was well until ten days before admission, when he suddenly became stuporous. Stupor and listlessness increased until the day of admission, when it was noticed that the child could not use his left arm and leg. Constipation, vague abdominal pains and loss of appetite were the only other symptoms. The child was well developed and well nourished. He was comatose but could be aroused. The head was

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4. There were a number of similar cases in which the spinal fluids gave a negative reaction, but these are not included in the table, since recovery did not occur and necropsy was not permitted, and hence it was impossible to ascertain the presence or absence of tuberculous meningitis.

turned to the left, and the left arm and leg were used little. The deep reflexes were hyperactive, the ankle clonus was sustained and more active on the left side, and the Babinski sign was positive on both sides. The neck was moderately stiff, but the Kernig sign was absent. Cheyne-Stokes respiration was present. The spinal fluid contained 125 cells, 66 per cent of which were mononuclears, and the Pandy reaction was positive. The tryptophan test was positive. No organisms were found on some six or seven careful examinations. Tuberculous meningitis, brain abscess and encephalitis were considered. The consultant neurologist thought encephalitis to be the most likely diagnosis and considered tuberculous meningitis to be only a bare possibility. Death occurred a week after admission.

Necropsy revealed tuberculous meningitis and miliary tuberculosis.

CASE 3 (case 2, table 2).—O. W., a colored child of 4 years, came to the Harriet Lane Home because of abdominal pain and severe vomiting of four hours' duration. The physical examination gave negative results save for a temperature of 101 F. The child was seen again the following evening. He had had practically no food, yet had vomited several times, and was said to have been delirious at night. At this time the temperature was 102 F., and the neck was stiff and the Kernig sign equivocal. He was admitted to the ward. The spinal fluid showed 200 cells, all mononuclears, and the Pandy reaction was positive. The diagnosis was tuberculous meningitis. The next day the spinal fluid contained 140 cells, 90 per cent of which were mononuclears. No tubercle bacilli were found. The tryptophan test was negative. The child was removed from the hospital against advice. He recovered, and he was later followed in the outpatient department.

Although from clinical examination it was felt that the child probably had tuberculous meningitis, in view of the negative tryptophan test a guarded prognosis was given, and the guardian was advised to have the child followed in the dispensary for at least three weeks. The child became quite well, and physical examination gave negative results when he was seen in the dispensary a month later.

CASE 4 (case 1, table 2).—E. A., a 5 year old colored girl, was admitted to the hospital on Sept. 26, 1929, with a history of substernal pain on inspirations and frequent nosebleeds during the first two weeks of August. She was well again until September 16, when she had another nosebleed. Two days later the substernal pain and the severe headaches recurred. There was loss of appetite. On September 21, the child began to vomit everything, became constipated and had periods of stiffness of the neck. She had a loose cough, but no whoop, although she was exposed to whooping cough. On admission, the patient was emaciated and drowsy, but irritable when aroused. The temperature was normal. The respirations were irregular. There was moderate general glandular enlargement, increased retromanubrial dulness and some dulness over the left upper lobe. The liver and spleen were palpable. There was a leukocytosis of 25,000 cells, 40 per cent of which were polymorphonuclear neutrophils. The spinal fluid pressure was increased. It contained 21 cells and gave a positive Pandy reaction. The tryptophan test was negative. The possibility of tuberculous meningitis was considered, although encephalitis of whooping cough origin was suggested by the white cell count and the presence of whooping cough in the family. The child developed bilateral Babinski and Kernig signs, stiffness of the neck, a positive Brudzinski and hyperactive reflexes. For two days generalized convulsions occurred.

The course was unchanged until October 16, when a paroxysmal cough developed. The diagnosis of encephalitis complicating pertussis was then made. The child was discharged well on Nov. 3, 1930.

CASE 5 (case 3, table 2).—C. T., a white boy, aged 9 years, was admitted to the hospital on July 18, 1929, with a history of headache, vomiting, malaise, drowsiness and restlessness. The child was said to have been "jumpy" for twenty-four hours. On examination he was found to be well developed and well nourished. His temperature was 103 F. He was drowsy and showed slow Cheyne-Stokes respirations, stiff neck, a positive Kernig sign and sluggish reflexes. The spinal fluid was under increased pressure and contained 196 cells, 85 per cent of which were mononuclear cells. The Pandy reaction was negative. Tuberculous meningitis, encephalitis and polio-encephalitis were considered. The tryptophan test, however, was negative. The child made an uneventful recovery, and when seen Aug. 27, 1929, he appeared to be well.

CASE 6 (case 4, table 2).—W. K., a 5 year old white boy, was admitted to the hospital on Aug. 6, 1929, with a history of fever, headache, restlessness, vomiting and pain in the region of the umbilicus for two days. On examination a general glandular enlargement, pain on flexion of the head, and pain on pressure over the occipital bone were found, but there was no rigidity of the neck. The spinal fluid was negative. Four days later the child had a positive Kernig sign and a stiff neck. Spinal fluid then showed 640 cells, with over 60 per cent mononuclears, and a positive Pandy reaction. The tryptophan test was negative. In view of the cellular findings and the negative tryptophan test, polio-encephalitis was considered, and convalescent poliomyelitis serum was given. The child was better the next day and made an uneventful recovery.

It is probable that in the very earliest stages of tuberculous meningitis the reaction to the tryptophan test is positive. B. S. (case 13, table 1), a 7 months old infant with advanced pulmonary tuberculosis, had a convulsion one evening during his long stay in the hospital. The onset of tuberculous meningitis was suspected. Spinal puncture revealed fluid with increased globulin and 120 cells per cubic millimeter. The fluid gave a distinctly positive reaction for tryptophan. The infant died twenty-four days later and autopsy showed tuberculous meningitis. It is most likely that the organisms had broken into the spinal fluid only a short time before the puncture was performed. As the disease progressed, subsequent fluids gave progressively more strongly positive reactions.

While the reaction is distinctly positive or negative in clear fluids, it may be confusing in xanthochromic or purulent fluids. Such confusion was encountered in thirteen cases not presented in the tables. The color developed was a peculiar purple rather than a delicate violet. In two of these, both new-born infants with signs of intracranial hemorrhage, proved by autopsy, the spinal fluids withdrawn after death were xanthochromic. In the others, the fluids were taken from patients having purulent forms of meningitis caused by the pneumococcus, meningococcus, staphylococcus and the influenza bacillus, as proved by culture alone or by culture and autopsy. However, the reaction with a purulent fluid can be distinguished from that given by a tuberculous fluid either by the shade of violet color or by the sensitivity and extent of the reaction.

The following cases illustrate this point. A patient was admitted to Sydenham Hospital for Contagious Diseases with signs of meningeal irritation. The first spinal fluid cell count was made by a student who reported 197 cells. No organisms were found. A diagnosis of encephalitis was considered. The tryptophan test was strongly positive, but showed the peculiar purple shade commonly given by purulent spinal fluids. The student's report was doubted, and a second spinal tap was made a few hours later. The spinal fluid contained 2,700 cells and numerous pneumococci. The child died, and autopsy confirmed the diagnosis of pneumococcus meningitis. On the other hand, F. S. (case 15, table 1) had 307 cells per cubic centimeter in the spinal fluid with 80 per cent polymorphonuclears, and at a subsequent tap, 900 cells with 94 per cent polymorphonuclear cells, yet in spite of the high count and the predominance of polymorphonuclear cells which would make one suspect quite strongly the presence of a purulent meningitis, the tryptophan reaction was delicate violet. The case proved to be one of tuberculous meningitis.

From the limited number of cases studied it seems that the tryptophan test may be of value in rapidly distinguishing a tuberculous from a nontuberculous meningitis. It is not to be relied on to the exclusion of well established diagnostic procedures, such as the demonstration of organism, guinea-pig inoculation, etc., since a tuberculous fluid may sometimes act negatively to the test and a nontuberculous fluid may give a positive reaction as pointed out by Aiello.[3]

SUMMARY AND CONCLUSIONS

1. Of seventy-eight fluids subjected to the tryptophan test, all (twenty-five) from cases of tuberculous meningitis, proved either by autopsy or guinea-pig inoculation, were positive. Of the fluids showing negative reaction, none was demonstrated to be from patients having tuberculous meningitis.

2. Purulent, xanthochromic and hemorrhagic spinal fluids gave a false but distinguishable positive reaction.

3. The test was of value as a diagnostic aid in the differential diagnosis of tuberculous meningitis and conditions that simulated it clinically or in spinal fluid findings.

HUMAN MILK STUDIES

VIII. A COMPARISON OF THE COMPOSITION OF THE MILK FROM THE TWO BREASTS *

MINERVA BROWN †

ICIE G. MACY

BETTY NIMS

AND

HELEN A. HUNSCHER

DETROIT

Observations on the relative percentage composition of milk from the two mammae of women have a dual importance: they add to our information concerning infant nutrition as well as to our knowledge of the physiology of milk secretion.

In earlier papers [1] several theories of the mechanism of milk secretion were reviewed and observations on the process in both animal and

* Submitted for publication, April 27, 1931.

* From the Nutrition Research Laboratories of the Merrill-Palmer School and the Children's Hospital of Michigan, Detroit.

†Miss Minerva Brown met an untimely death in 1929.

1. (*a*) Macy, I. G.; Outhouse, J.; Long, M. L., and Graham, A.: Human Milk Studies: I. Technique Employed in Vitamin Studies, J. Biol. Chem. **73**:153, 1927; (*b*) II. The Quantitative Estimation of Vitamin A, ibid. **73**:175, 1927; (*c*) III. The Quantitative Estimation of Vitamin B, ibid. **73**:189, 1927. (*d*) Outhouse, J.; Macy, I. G.; Brekke, V., and Graham, A.: IV. A Note on the Vitamin A and B Content of Cow's Milk, ibid. **73**:203, 1927. (*e*) Outhouse, J.; Macy, I. G., and Brekke, V.: V. A Quantitative Comparison of the Antiricketic Factor in Human and Cow's Milk, ibid. **78**:129, 1928. (*f*) McCosh, S. S.; Macy, I. G., and Hunscher, H. A.: VI. Vitamin Potency as Influenced by Supplementing the Maternal Diet with Yeast, ibid. **90**:1, 1931. (*g*) Macy, I. G., and Outhouse, J.: Breast Milk: A Variable Food, J. Am. Dietet. A. **4**:9, 1928; (*h*) The Vitamin Content of Milk Used in Infant Feeding, Am. J. Dis. Child. **37**:379 (Feb.) 1929. (*i*) Macy, I. G.; Hunscher, H. A.; Nims, B., and McCosh, S. S.: Metabolism of Women During the Reproductive Cycle: I. Calcium and Phosphorus Utilization in Pregnancy, J. Biol. Chem. **86**:17, 1930. (*j*) Hunscher, H. A.: II. Calcium and Phosphorus Utilization in Two Successive Lactation Periods, ibid. **86**:37, 1930. (*k*) Macy, I. G.; Hunscher, H. A.; McCosh, S. S., and Nims, B.: III. Calcium, Phosphorus, and Nitrogen Utilization in Lactation Before and After Supplementing the Usual Home Diets with Cod-Liver Oil and Yeast, ibid. **86**:59, 1930. (*l*) Hunscher, H. A.; Vincent, L., and Macy, I. G.: Psychophysiological Studies: I. The Technique of Securing Quantitative and Coordinated Psychological and Physiological Data on Lactating Women in Their Usual Home Environment, Child Development **1**:15, 1930. (*m*) Shukers, C. F.; Macy, I. G.; Donelson, E.; Nims, B., and Hunscher, H. A.: Sources of Nutrients Chosen by Women During

man were discussed. Analogous studies on the milk obtained from the different quarters of the udder of the cow demonstrated that the milk was similar but not identical in composition.[2] It was suggested that the quarters of the udder of the cow show not only anatomic individuality but differences in the physiology of milk formation. Schnorf [3] noted, however, that the two forequarters and the two hindquarters of the mammary gland of the cow appeared to function alike.

It would seem that similarity in percentage composition would indicate uniformity in the rate and magnitude of the activity of the secreting cells of the mammary gland, which function in the release of the milk products. Gross differences in the quality of milk secreted simultaneously by the two breasts of the same woman have been reported in the literature.[4] Originally, dissimilarity in the composition of milk secreted by the two breasts was suggested by accounts of infants who failed to thrive when nursed exclusively from one breast and thrived when transferred to the milk of the opposite breast. These earlier observations, however, were seldom accompanied by a satisfactory analysis of the milk, although differences in the appearance of the milk from the two breasts, particularly in color, were noted occasionally.[5]

Similar clinical observations later stimulated more detailed chemical investigations, not only in cases in which complications in the nutritional status of the baby suggested variations in the milk from the two

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2. Proks, J.: The Individuality of the Mammary Glands of the Cow, Proc. of 8th World's Dairy Congress, 1928, Lait **8**:553, 1928; The Individuality of the Quarters of the Cow's Udder, Chem. Abstr. **23**:892, 5497, 1929. Benton, A. G.: Variations in the Milk from Different Quarters of the Same Udder: Their Significance in Studies of Coagulability, J. Dairy Sc. **12**:481, 1929.

3. Schnorf, C.: Neue physikalisch-chemische Untersuchungen der Milch Unterschiedung physiologischer und pathologischer Kuh-Milch, Zurich, O. Fussli, 1905; cited by Jackson and Rothera: Biochem. J. **8**:1, 1914.

4. Thiemich, M.: Ueber Veränderung der Frauenmilch durch physiologische und pathologische Zustände, Monatschr. f. Geburtsh. u. Gynäk. **8**:521, 645, 1898. Sourdat, L.: Observation d'une inégale production et d'une différence de composition du lait pour lex deux seins de la même femme, Compt. rend. Soc. de biol., 1870; cited by Thiemich. Brunner, T.: Ueber die Zusammensetzung der Frauenmilch, Arch. f. d. ges. Physiol. **7**:440, 1873; cited by Thiemich.

5. Varges, J.: Ueber die chemische Einwirkung des Laktagols auf die Zusammensetzung der Frauenmilch, Med. Klin. **1**:229, 1905.

breasts, but also in cases in which no nutritional disturbances were encountered.[6] Zappert and Jolles[7] reported an interesting case in twins, each accustomed to being fed exclusively from a given breast, which seems typical of the early clinical observations. The condition of the one twin, who was weak and undernourished, improved when he was transferred to the opposite breast, while the other twin, who was hearty and strong, suffered nutritional impairment through such an exchange. This observation was accompanied by an analysis of the milk from both breasts which demonstrated that the milk of the left breast was richer in composition than that of the right.

Although occasional analyses have been reported from time to time, little attention has been focused on the physiologic or clinical significance of the nonuniformity of the milk obtained from the two glands. Furthermore, the earlier studies reported in the literature were conducted under heterogeneous and unstandardized methods of milk collection, sampling and analysis, and these various factors must be taken into account in considering the gross discrepancies observed in the composition of the milk from the two breasts. Sikes[8] suggested that if determinations are made under standardized methods of milk sampling, and if the mother produces an ample milk supply, little discrepancy should be found in the percentage composition of the milk from the two breasts.

Faced by the clinical findings in the early literature, which were generally obtained under desultory methods, and confronted by numerous questions concerning the clinical and physiologic import of differences in the activity of the two glands, one wonders if the observed dissimilarities are a sequel of abnormal functioning and anomalies inherent in the mammae themselves or are characteristic of normally functioning glands.

As an integral part of a series of studies on the chemistry of human milk,[1a-n] it was the object of the present study to determine, under rigidly standardized methods of expression and analysis,[10] the

6. Johannessen, A.: Studien zur Sekretionsphysiologie der Frauenmilch, Jahrb. f. Kinderh. **39**:380, 1895. Mendes de Leon, M. A.: Ueber die Zusammensetzung der Frauenmilch, Ztschr. f. Biol. **17**:501, 1881; cited by Thiemich. Adriance, V., and Adriance, J. S.: A Clinical Report on the Chemical Examination of Two Hundred Cases of Human Breast Milk, Arch. Pediat. **14**:22, 1897. Guiraud, F.: Nouvelles considerations chemiques, physiologiques, et cliniques sur le lait de femme dans l'état de sante; abstr., Arch. Clin. de Bordeaux **6**:291, 1897; cited by Thiemich. Schlossmann, A.: Zur Frage der natürlichen Säuglingsernährung, Arch. f. Kinderh. **30**:288, 1900; **33**:338, 1902.

7. Zappert, J., and Jolles, A.: Ueber Untersuchungen der Milch beider Brüste, Wien. med. Wchnschr. **53**:1913, 1903.

8. Sikes, A. W.: On the Phosphorus and Calcium of Human Milk, J. Physiol. **34**:464, 1906.

corresponding percentage composition of milk secreted by the two breasts in three lactating women; to relate any differences in composition to the physiology of milk secretion and to the nutrition of the infant, and to evaluate the clinical significance of these findings.

PROCEDURE

In order to study the composition of the milk closely representative of a simultaneous secretion, the two breasts were completely emptied by manual expression within a fifteen minute period at regular four hour intervals throughout the day and night. In this way, any effect of the nursing baby on the activity of the glands was entirely eliminated and such other factors as the time interval between emptying, the breasts, the magnitude of mechanical stimulation and the influences of food, activity and emotion were similar for both glands. Furthermore,

TABLE 1.—*History of Subjects*

Observation	Subject 6		Subject 7,	Subject 8,
	Lactation A	Lactation B	Lactation A	Lactation B
Age	25	27	33	29
Height, inches	62.2	62.2	68.5	62.6
Pregnancy	3	4	2	2
Birthweight of baby	7 lb., 8 oz.	8 lbs., 10 oz.	8 lbs., 3 oz.	6 lbs., 12 oz.
Date of birth of baby	Oct. 13, 1926	Aug. 20, 1928	Nov. 20, 1926	July 16, 1928
Date of study	(a) Feb. 15, 1927, 18th week (b) Dec. 8, 1927, 60th week	(c) Oct. 21, 1929, 63rd week	(a) Feb. 1, 1927, 10th week (b) Nov. 1, 1927 50th week	(a) Sept. 24, 1929, 63rd week
Weight at time of study, Kg	(a) 65.4 (b) 64.0	(c) 65.4	(a) 65.0 (b) 64.0	(a) 81.3
Average daily milk output	2,600 cc.	3,134 cc.	2,000 cc.	1,419 cc.

the subjects (histories given in table 1), who were at this time selling their excess milk to the Mothers' Milk Bureau of Detroit, were accustomed to expressing all of their milk by hand and could empty both breasts, with equal efficiency. Subject 6 had expressed all of her milk through three complete lactation periods of fourteen months each; subjects 7 and 8, through one lactation period. Their proficiency insured the collection of samples that represented a complete removal of the milk from the breasts at each expression period. Since the subjects had been accustomed to expressing all of their milk manually and feeding it to their babies by bottle continuously throughout the entire lactation period, the stimulation afforded by the suckling of the infant cannot be said to play a rôle in these studies. The subjects were secreting large quantities of milk, so that the conditions of an ample milk flow, necessary for an accurately conducted study, were maintained.

EXPERIMENTAL WORK

In table 2 are recorded the daily average values of certain constituents of the milk from the right and left breasts of each subject. These data demonstrate that samples of milk representative of the total daily secretion from the right and left breasts of the same woman are similar in composition.

The percentage concentration of fat in corresponding samples of the milk approaches uniformity, as shown by the average per cent of difference, 0.8 per cent. Denis and Talbot,[9] on the contrary, observed that samples of human milk taken from the two breasts at the same time tended to have the same composition except in the percentage of

TABLE 2.—*Comparative Percentage Composition of Human Milk Representative of Twenty-Four Hour Production, Collected at Four Hour Intervals Simultaneously from the Right and the Left Breasts* *

Observation		Fat			Lactose			Protein			Total Solids			Calories per 100 Cc.		
Subject	Study	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference
6	(a) av. 4 hr.....	4.30	4.29	0.2	7.26	7.33	0.8	1.089	1.083	0.5	12.29	12.24	0.4	72	72	...
6	(b) 24-hr.....	4.22	4.22	...	6.80	6.86	0.9	1.116	1.104	1.0	12.72	12.73	0.1	70	70	...
6	(c) av. 4 hr.....	4.25	4.26	0.3	6.88	7.10	3.0	0.920	0.938	1.9	12.18	12.48	2.4	70	71	1.4
7	(a) av. 4 hr.....	3.88	3.91	0.8	7.19	6.67	6.9	0.968	0.981	1.3	11.52	11.53	0.1	68	66	3.0
7	(b) 24-hr.....	4.62	4.63	0.2	6.82	6.75	1.0	1.162	1.166	0.3	13.18	13.04	1.0	74	73	1.3
8	(a) av. 4 hr.....	5.81	5.63	3.1	7.12	7.13	0.1	1.169	1.181	1.0	14.28	14.14	0.9	86	84	2.3
Average per cent difference			0.8			2.1			1.0			0.8			1.3	

Observation		Solids Not Fat			Total Ash			Calcium			Phosphorus			Ca:P Ratio		
Subject	Study	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference	Left	Right	Per Cent Difference
6	(a) av. 4 hr.	7.99	7.97	0.2	0.205	0.207	1.0	0.0344	0.0340	1.2	0.0135	0.0131	3.0	2.6	2.6	...
6	(b) 24-hr....	8.50	8.51	0.1	0.202	0.197	2.4	0.0306	0.0302	1.2	0.0132	0.0130	1.5	2.3	2.3	...
6	(c) av. 4 hr.	7.93	8.22	3.5	0.183	0.181	1.1	0.0285	0.0283	0.7	0.0123	0.0125	1.6	2.3	2.2	4.1
7	(a) av. 4 hr.	7.64	7.62	0.2	0.197	0.200	1.5	0.0295	0.0304	2.3	0.0138	0.0141	2.1	2.1	2.2	4.4
7	(b) 24-hr....	8.56	8.41	1.7	0.174	0.173	1.4	0.0224	0.0234	4.3	0.0163	0.0166	1.8	1.4	1.4	...
8	(a) av. 4 hr.	8.47	8.51	0.5	0.174	0.180	2.9	0.0255	0.0259	1.5	0.0141	0.0136	3.5	1.8	1.9	5.0
Average per cent difference.....			1.0			1.7			2.0			2.3			2.3	

* The values for fat, lactose, protein, etc., are given in grams per hundred cubic centimeters. Six complete analyses of the milk from each breast were made at every four hour interval throughout the day and night, and the averages of the six, representative of the complete twenty-four hour composition of milk from each breast, are recorded in the table. Analyses of the milk in studies *b* on subjects 6 and 7 were made on a single complete twenty-four hour pooled collection of milk from each breast, pumped at regular four hour intervals during the day and night.

fat, which differed greatly in some instances. Studies *a* on subjects 6 and 7 demonstrate identical rhythmic secretion of fat, total solids and solids-not-fat in the milk expressed from the two glands during an entire day. The curves of chart 1 show the concentration in grams of fat, total solids and solids not fat per hundred cubic centimeters of the milk of the right and left breasts of the two subjects at four hour

9. Denis, W., and Talbot, F. B.: A Study of the Lactose, Fat and Protein Content of Women's Milk, Am. J. Dis. Child. **18**:93 (Aug.) 1919.

intervals. The curves representing the grams of fat per hundred cubic centimeters of milk from the two breasts of subject 6 are practically superimposed, showing equivalence not only in the relative rate of change during the day but also in absolute values. Although the curves representing the concentration of fat in the milk of subject 7 present a picture different from that in the case of subject 6, the breasts of

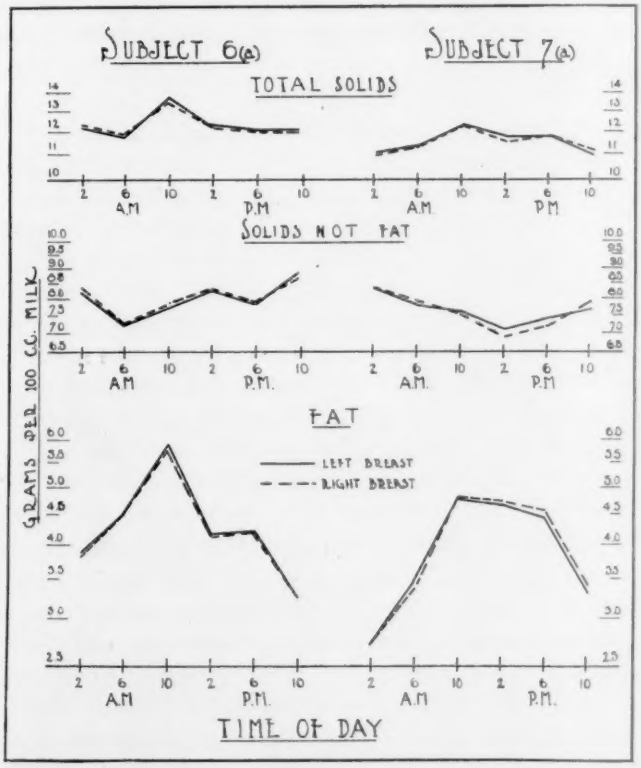

Chart 1.—Graph showing the similarity in percentage composition of milk simultaneously expressed from the right and left breasts at four hour intervals throughout the day and night. The time of day is plotted arithmetically and the grams per hundred cubic centimeters logarithmically, thus illustrating not only the absolute values but the relative rate of change of values throughout the day.

subject 7 also seem to function identically in their secretion of fat. The semblance of unity in the corresponding curves of the solids not fat further suggests uniform functioning of the two glands, and still other indications of similarity of secretion are given by the near identity of the corresponding curves representative of the total solids in the milk from each breast. The synthesis and secretion of milk fat have

been studied extensively.[10] It has been declared that these processes are governed by a mechanism entirely separate from that regulating other milk constituents, although the actual processes involved remain obscure. The formation of fat has been attributed to a breaking away and degeneration of mammary gland cells.[11] However, simultaneous secretion by the two glands of milk identical in fat concentration would imply that such a degeneration would proceed at the same rate and magnitude in both breasts. Consequently, the data presented may offer convincing evidence against theories of the derivation of milk fat from cell degeneration, and evidence for theories of the formation of milk fat by processes of cellular secretion.

The similarity in the composition of the solids in the milk secreted from the two breasts throughout the day, as shown in chart 1, indicates that the activity of the two glands is governed similarly in this respect. The functioning of the glands appears to be uniform and accordingly to be influenced similarly by such factors as food, environment and emotion. The averages of the protein and lactose content of the milk from the two breasts tended toward equivalence, though there were greater differences in some samples than in others. An average of 0.8 per cent of difference in total solids and 1 per cent in solids not fat in corresponding samples of milk from the two glands further indicates a uniformity in the secretion of solid constituents, fat, lactose, protein and ash. The equivalent caloric values per hundred cubic centimeters of the total daily output of milk from the left and right breasts also demonstrate the similarity in percentage composition.

The percentage concentration of certain milk constituents and the milk volume are usually considered to be directly associated, i. e., solids not fat are considered to be directly proportional and fat inversely proportional to the quantity of milk produced.[12] Consequently, the relation between the volumes of milk expressed from each breast at each four hour interval and their respective percentage compositions presents a pertinent issue. The quantities of milk obtained at four hour intervals from each breast are represented by the curves of chart 2. Though the amounts of milk obtained from the two glands of subject 6 followed a similar rhythm during the day, the right breast

10. Petersen, W. E.; Palmer, L. S., and Eckles, C. H.: The Synthesis and Secretion of Milk Fat: I. The Time of Milk and Fat Secretion, Am. J. Physiol. **90**:573, 1929; II. An Analytical Study of the Fat of the Bovine Mammary Gland, ibid. **90**:582, 1929; III. A Study of the Activity of the Perfused Surviving Gland with Special Reference to the Fat, ibid. **90**:592, 1929.

11. Marshall, F. H. A.: The Physiology of Reproduction, ed. 2, New York, Longmans, Green & Company, 1922, p. 591.

12. Cockefair, E. A.: The Activity of the Mammary Gland as Determined by Analysis of Mammary Gland Before and After Milking, J. Dairy Sc. **11**:230, 1928.

consistently produced more milk than the left, and yet the milk of the two breasts appeared identical in the percentage composition of fat, solids not fat and total solids. On the other hand, though the left breast of subject 7, produced more milk than the right, and the amounts of milk secreted by the two glands showed no uniformity in rhythm, the percentage concentration of solid constituents was similar in the milk of the two glands. It would seem, therefore, that the percentage composition of the milk secreted by the two glands is not a correlative of the respective gland capacity and subsequent milk volume.

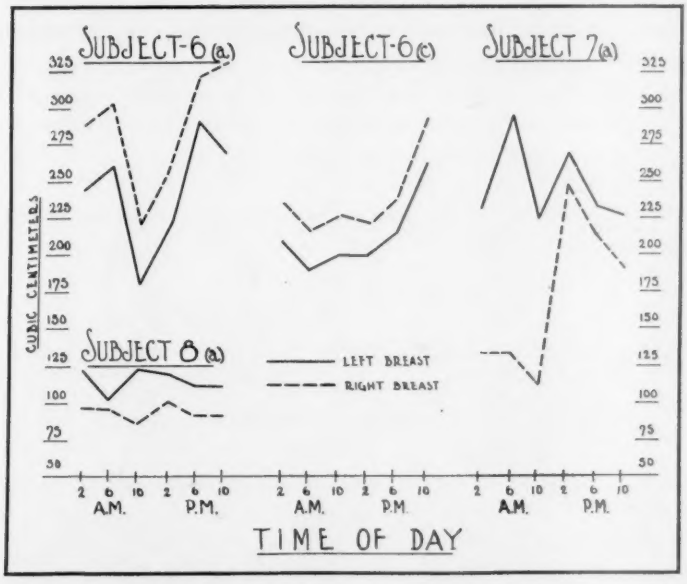

Chart 2.—Graph showing the volume of milk expressed from the right and left breasts at four hour intervals throughout the day and night.

The total volume of milk secreted by each breast during a twenty-four hour day is recorded in table 3. The daily total quantities of milk secreted by the two glands show differences as great as 346 cc. The total amounts of fat, protein, carbohydrate and associated energy value produced in a single day by the two breasts may be quite different. This difference is strikingly demonstrated in the case of subject 7, whose left breast during one day secreted milk containing 13.1 Gm. of fat, 3.2 Gm. of protein, 30.8 Gm. of carbohydrate and 254 calories more than that secreted by the right breast. The nutritional significance of such gross differences is immediately apparent. Even though the milk may not differ in actual percentage composition, the total amount of nutrients furnished by the two mammae may vary considerably even under rigidly controlled and standardized conditions. It is logical to

expect greater inequalities in total volume output when the baby is the chief performer in securing the milk. Such findings are significant in considering the nutritional status of infants nourished exclusively on the milk from one breast. It is important, then, to consider not only the relative percentage composition but also the total quantity of milk and milk constituents available to the infant from each breast. The common practice of nursing the baby at alternate breasts at alternate feeding periods likewise demands inspection in terms of the relative capacity of the two breasts and the total amount of nutrients furnished. In our subjects the percentage concentration of total ash, calcium and phosphorus in the milk of the two breasts is in general uniform though

TABLE 3.—*The Total Volume of Milk Secreted by the Right and Left Breasts During the Twenty-Four Hour Day and a Partial Analysis of the Constituents*

Observation		Volume, Cc.			Fat, Gm.			Protein, Gm.			Carbohydrate, Gm.			Total Calories		
Subject	Study	Left	Right	Difference	Left	Right	Difference	Left	Right	Difference	Left	Right	Difference	Left	Right	Difference
6	(a)	1,471	1,740	269	63.3	74.6	11.3	16.0	18.8	2.8	106.8	127.5	20.7	1,061	1,257	196
6	(b)	1,000	1,122	122	42.2	47.4	5.2	11.2	12.4	1.2	68.0	77.0	9.0	697	784	87
6	(c)	1,279	1,238	41	54.4	52.7	1.7	11.8	11.6	0.2	88.0	87.9	0.1	888	873	15
7	(a)	1,490	1,144	346	57.8	44.7	13.1	14.4	11.2	3.2	107.1	76.3	30.8	1,007	753	254
7	(b)	673	624	49	31.1	28.9	2.2	7.8	7.3	0.5	45.9	42.1	3.8	495	458	37
8	(a)	691	565	126	40.2	31.8	8.4	8.1	6.7	1.4	49.2	40.3	8.9	501	474	117

these values do not approach equality as do some of the other constituents. Some of the four hourly samples show a perceptible difference in the percentage composition of these factors in the milk of the two breasts, but for the most part analogous samples show a close correspondence in this respect. The average percentage differences of ash, calcium and phosphorus for corresponding twenty-four hour samples of milk from the two breasts were 1.7, 2 and 2.3, respectively. The constancy of the calcium : phosphorus ratio further demonstrates the similarity in quality of corresponding milk samples expressed from the two glands.

There is little literature concerning the mineral and ash constituents of human milk, particularly concerning analogous samples of milk taken simultaneously from the two mammary glands. In three cases Sikes [8] studied he found the phosphorus content of milk from the two breasts to be similar, with values as follows: 0.0216 and 0.0103; 0.0104 and 0.009; 0.0114 and 0.0114. In studies of the iron in human milk, including determinations of the secretion of this element in the milk

of the two breasts, Dorlencourt and Calugareanu-Nandris [13] found the rhythms of iron secretion in the two breasts to be quite different.

Earlier speculations suggested that differences in the quality of milk from the two mammae were to be expected as the natural sequel of their relative anatomic position in relation to the blood supply. Mendes de Leon [14] suggested that milk from the right gland would always be more concentrated than that from the left, owing to its position of priority with respect to securing the necessary constituents from the blood. However, determinations made by Zappert and Jolles [7] showed, on the contrary, that in nine of the ten cases they studied the left gland secreted a more concentrated milk than the right. Although diverse opinions followed, it is nevertheless interesting to study the data from this angle.

TABLE 4.—*Summary of All Analyses of Milk Secreted by Right and Left Breasts* *

Constituent	Right Breast			Left Breast		
	Minimum	Maximum	Average	Minimum	Maximum	Average
Fat	2.68	7.10	4.49	2.69	6.71	4.51
Lactose	6.57	7.83	6.97	6.53	7.55	7.01
Total solids	11.02	15.07	12.69	11.04	15.20	12.69
Solids not fat	6.89	9.15	8.21	7.10	8.88	8.18
Total nitrogen	0.142	0.199	0.169	0.134	0.200	0.168
Total ash	0.167	0.222	0.190	0.160	0.214	0.189
Calcium	0.0220	0.0368	0.0287	0.0224	0.0365	0.0285
Phosphorus	0.0119	0.0160	0.0138	0.0120	0.0151	0.0139

* The values are given in grams per hundred cubic centimeters.

In table 4, the averages of all analyses of the composition of the milk from the right breast are compared with those of the milk from the left breast. The corresponding average values for the right and left breasts are practically identical, demonstrating that in these three women the milk of the two breasts, as studied under a carefully controlled technic of milk expression and analysis, showed no consistent discrepancy in concentration, as earlier investigations suggested might be the case.

Eldson [15] reported analyses of the average relative composition of the milk from the two mammae of numerous subjects (table 5).

Myers [16] recently reported extensive studies on the milk from the left and right breasts of many women, and presented data concerning range of variation and average values (table 6).

13. Dorlencourt, H., and Calugareanu-Nandris: Le fer dans le lait de femme; son dosage; ses variations, Bull. Soc. de pediat. de Paris **24**:376, 1926; Recherche sur l'élimination du fer médicamenteux par la glande mammaire, Compt. rend. Soc. de biol. **95**:1040, 1926; abstr., J. A. M. A. **88**:64 (Jan. 1) 1927.

14. Mendes de Leon (footnote 6).

15. Eldson, G. D.: The Composition of Human Milk, Analyst **53**:78, 1928.

16. Myers, B.: An Investigation on the Analysis of Human Milk, Brit. J. Child. Dis. **24**:249, 1927.

Our observations demonstrate close similarity in the percentage composition of milk from the two breasts and therefore uniformity in their cellular activity. However, the special conditions under which the studies were conducted must be considered. The subjects had been accustomed to pumping their own milk from the breasts, and consequently were sufficiently skilled to guarantee complete removal of the milk. Furthermore, during the entire lactation period prior to the studies, as well as during the studies, the infant imposed no modifications on the glands in obtaining his necessary nourishment. This study demonstrates the fact that identity can occur in the milk secreted by the two breasts, i. e., an equivalence which may be the optimum limit of perfection approached by normal functioning glands is possible.

TABLE 5.—*Results of Eldson*

	Number of Cases	Solids Not Fat per Cent			Fat, per Cent		
		Max.	Min.	Av.	Max.	Min.	Av.
Left breast	244	11.7	3.8	8.73	10.2	0.4	3.23
Right breast	217	11.4	5.2	8.78	8.0	0.8	3.27

TABLE 6.—*Results of Myers*

	Right Breast, per Cent		Left Breast, per Cent	
	Variations	Average	Variations	Average
Protein	0.68 to 3.42	1.64	0.72 to 3.89	1.73
Fat	1.56 to 6.44	3.59	0.99 to 6.86	3.49
Lactose	2.16 to 7.54	6.06	4.84 to 8.06	6.19
Salts	0.08 to 0.56	0.19	0.06 to 0.40	0.21

Although our data indicate remarkable uniformity in the two glands in the rate of milk formation and the resulting percentage composition of the milk, they demonstrate also an inequality in the relative capacity and resulting milk volume of the two breasts. Presumably, gross inequalities in the total volume output of the two glands would occur also when the infant is the operator in securing the milk, so the total quantity of constituents available in the milk from the two breasts may differ considerably.

In considering the previously reported dissimilarity of the milk secreted by the two mammae of a subject, several questions present themselves. It is frequently suggested that milk composition seems to adjust itself to the condition of the nursing infant. It is known that less frequent emptying of the glands seems to diminish cellular activity, with resulting decrease in quantity output.[17] It has been observed

17. Ragsdale, A. C.; Turner, C. W., and Brody, S.: The Rate of Milk Secretion as Affected by an Accumulation of Milk in the Mammary Gland, J. Dairy Sc. **7**:249, 1924. Schnorf (footnote 3) and Cockefair (footnote 12).

also that, owing to reabsorption processes, the milk tends to change when it remains in the gland for any length of time.[18] In this manner the milk may tend to become inferior in quantity and quality in the case of an underweight, weak baby unable to strip the breasts completely. Measurements of the electric conductivity and depression of the freezing point of human milk, which are physical constants influenced by such substances in the milk as lactose and mineral salts, have confirmed the idea that the quality of milk is controlled by the nursing infant.[19] Such observations suggest the possibility that lack of uniformity in the composition of the milk secreted from the two breasts may result from differences in the degree of mechanical stimulation and pressure applied to the glands.

In view of these facts the difficulties in the way of reproducing any given set of conditions governing the quality of milk the suckling child receives—even of simulating the conditions imposed by the child himself—are obvious; so that the practical application of experimental studies to nutritional problems of infant feeding is indeed an enigma. It is hoped, however, that data of this kind will be found not only to have a clinical significance in these problems but also to suggest clues bearing on certain problems of milk formation and secretion.

CONCLUSION

Under carefully controlled conditions of milk expression and analysis, and on the basis of samples taken at each four hour interval during the twenty-four hour day, it has been demonstrated that in three women the two mammae secreted milk uniform in the percentage concentration of fat, protein, lactose, total solids, solids not fat, total ash, calcium and phosphorus. The two breasts functioned differently in the total production of milk and milk nutrients.

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18. Porcher, C.: Arch. de méd. d. enf. **23**:569, 625, 1920; Retention of Breast Milk, abstr., J. A. M. A. **75**:1750 (Dec. 18) 1920. Davidson, F. A.: The Effect of an Incomplete Removal of Milk from the Udder on the Quantity and Composition of the Milk Produced During the Immediate Subsequent Milkings, J. Dairy Sc. **7**:267, 1924.

19. Jackson, L. C., and Rothera, A. C. H.: Milk, Its Sugar, Conductivity, and Depression of Freezing Point, Biochem. J. **8**:1, 1914.

AVITAMINOSIS AND BLOOD CLOTTING FUNCTION *

I. NEWTON KUGELMASS, M.D.
AND
EMMA LOUISE SAMUEL, B.S.
NEW YORK

Dietary protein accelerates blood coagulability, while dietary carbohydrate and minerals retard it to the extent of producing manifestations of bleeding in the course of illness or surgical intervention. The question arises whether the gross dietary constituents alter the clotting mechanism of the blood or whether associated vitamins induce these changes. Consistent clinical observation has led to the conclusion that the clotting time is not a definite criterion of blood clotting function, and so we [1] have developed methods for the determination of the clotting constituents as a basis for evaluating the clotting status of the blood under varying conditions. The rôle of vitamins in the synthesis and maintenance of clotting components in the blood has been determined by a systemic study of the effect of specific vitamin deficiency diseases in rats on the blood clotting function measured quantitatively.

Four groups of rats of the same stock were maintained on dietary rations free from vitamin A, vitamin B complex, vitamin D and vitamin E, respectively. Vitamin C-free dietaries were given to young guinea-pigs. Determinations of the clotting components of the blood were made during a preliminary normal regimen and subsequently after definite manifestations of specific vitamin deficiency disease became apparent.

EFFECT OF DEFICIENCY IN VITAMINS

Vitamin A Deficiency.—The effect of vitamin A deprivation on the changes in the blood with respect to its clotting constituents was first studied by Cramer [2] in England. He maintained rats on a dietary deficient in vitamin A in both light and darkness, and concluded that ultraviolet irradiation stimulated the production of blood platelets and that vitamin A participated in their formation. This work was done

* Submitted for publication, May 5, 1931.

* From the Department of Pediatrics, the Fifth Avenue Hospital.

1. Kugelmass, I. N.; Bancroft, F. W., and Stanley-Brown, M.: The Determination and Regulation of Blood Clotting Function in Childhood, Am. J. Dis. Child. **39**:471 (March) 1930.

2. Cramer, W.: Lancet **1**:963, 1922.

in 1922, before vitamins A and D were differentiated, and so the interpretation of the data must necessarily be revised in the light of present knowledge.

The vitamin A-free diet on which our group of rats was maintained consisted of casein, 20 per cent; lard, 24 per cent; Osborne and Mendel salt mixture, 4 per cent; agar, 2 per cent, and starch and yeast, 5 per cent, given separately from the food each day. The vitamin A deficiency becomes manifest initially by failure to gain in weight and then by steady decline in weight to the extent that the rat becomes emaciated, its disposition ugly and the extremities cyanotic. There is a recurrence of infection of the upper respiratory tract, with obvious conjunctival and nasal congestion and wheezy respiration.

TABLE 1.—*Blood Clotting Components in Vitamin A Deficiency*

Date	Determination	Prothrombin	Fibrinogen	Antithrombin	Platelets		Index
					Concentration	Lysis, per Cent	
9/18/30	Predietary	1.0	0.4	1.0	525,000	45	0.4
10/16/30	Postdietary	1.0	0.4	1.0	520,000	45	0.4
10/28/30	Postdietary	1.0	0.4	1.0	520,000	44	0.4
11/ 6/30	Postdietary	1.0	0.36	1.0	490,000	38	0.35
12/23/30	Postdietary	0.85	0.24	1.0	480,000	37	0.20
9/25/30	Predietary	1.0	0.5	1.0	510,000	48	0.5
10/12/30	Postdietary	1.0	0.5	1.0	520,000	45	0.5
10/30/30	Postdietary	1.0	0.45	1.0	500,000	40	0.45
11/10/30	Postdietary	0.9	0.35	1.0	490,000	45	0.4

The blood taken before the introduction of the vitamin A deficient diet shows normal values for each of the components involved in the clotting mechanism as contrasted with those observed in children. However, in rats the number of platelets fluctuates at about 500,000 per cubic millimeter, which is twice the level of that observed normally in children. Vitamin A deficiency in the dietary produces no change in any of the constituents involved in coagulation, even after two months of deprivation of vitamin A. Beyond that period, we have observed first a diminution in the fibrinogen content to about half the inital value after the third month of vitamin A restriction and then a slight decrease in the prothrombin content and in the number of platelets. The striking effect is the diminution in the fibrinogen content after prolonged deprivation of vitamin A when nutritional dystrophy characterizes the state of the animal. The clotting index is half of the normal one, paralleling the decrease in the fibrinogen concentration. Vitamin A deficiency evidently produces no change in any of the clotting constituents, not even in the platelets. The subsequent

diminution in the fibrinogen is a consequence of nutritional atrophy rather than a concomitant of vitamin A deprivation.

Vitamin B Deficiency.—The literature reveals no investigation relating any rôle of vitamin B to the blood clotting mechanism. The vitamin B-free diet consisted of casein, 20 per cent; starch, 60 per cent; lard, 15 per cent; Osborne and Mendel salt mixture, 5 per cent, and cod liver oil, 1 drop, daily.

Animals deprived of vitamin B showed, after eight weeks, not only failure to grow but actual loss of weight, loss of appetite, fall in temperature, a huddling posture, poor musculature, matted fur, bluish extremities and putrefactive stools. They survived the drawing of blood for the determination of clotting components; they were then given an adequate dietary.

TABLE 2.—*Blood Clotting Components in Vitamin B Deficiency*

Date	Determination	Pro-thrombin	Fibrinogen	Anti-thrombin	Platelets		Index
					Concentration	Lysis, per Cent	
9/18/30	Predietary	1.0	0.4	1.0	560,000	45	0.4
10/14/30	Postdietary	1.0	0.28	1.0	545,000	45	0.3
10/21/30	Postdietary	1.0	0.28	1.0	500,000	45	0.3
10/27/30	Postdietary	1.0	0.28	1.0	475,000	44	0.3
9/25/30	Predietary	1.0	0.5	1.0	540,000	45	0.5
10/12/30	Postdietary	1.0	0.25	1.0	520,000	45	0.3
11/10/30	Postdietary	1.0	0.24	1.0	500,000	45	0.3

A vitamin B deficient dietary produced no change in any of the clotting components, except in the fibrinogen content immediately after elimination of the B complex from the daily regimen, but this alteration was not sufficient to produce manifestations of bleeding. The decrease in fibrinogen is obviously an expression of nutritional atrophy in that the rate of regeneration by the liver is impaired.

Vitamin C Deficiency.—Previous workers have made studies of histologic changes occurring in the course of scurvy, but with little reference to actual changes in the blood clotting constituents. The vitamin C-free diet was given to young guinea-pigs weighing from 250 to 300 Gm. The diet consisted of rolled oats and hay heated to 105 C. for four hours, 20 cc. of pasteurized milk and water given freely.

In animals deprived of vitamin C scurvy appeared after the second week, as evidenced by squeals when the tender joints were touched, loss of muscle tone, loss of weight, huddled posture and persistent lethargy. Autopsy on pig 701 showed hemorrhage in the hip joint of one hind leg and in the knee joint of the other; however, only slight swelling was observed in the forelegs, and there was no hemorrhage in

any other organ. The teeth were brittle and the bones of the hind legs were particularly so. The heart showed a thrombus, and the right ventricle was ruptured by a large blood clot. Pig 702, which was cured of scurvy but died later in the course of another experiment, showed a slight hemorrhage in the joints but none in other organs, and the teeth and bones were no longer brittle.

Vitamin C deficiency in the dietary produces no change in the clotting components of the blood. The hemorrhage characterizing scurvy is extravasation of blood from actively functioning cells as a result of the degeneration of the capillary endothelium. These changes are vascular rather than alterations in the character of blood clotting components or in the tissues that generate these potential clotting substances.

TABLE 3.—*Blood Clotting Components in Vitamin C Deficiency*

Date	Determination	Prothrombin	Fibrinogen	Antithrombin	Platelets		Index
					Concentration	Lysis, per Cent	
9/17/30	Predietary	1.0	0.64	1.0	185,000	38	0.65
10/ 3/30	Postdietary	1.0	0.54	1.0	170,000	32	0.55
11/10/30	Postdietary	1.0	0.52	1.0	180,000	30	0.55
9/25/30	Predietary	1.0	0.60	1.0	180,000	40	0.60
10/30/30	Postdietary	1.0	0.55	1.0	170,000	35	0.55
10/28/30	Predietary	1.0	0.54	1.0	180,000	33	0.55
11/20/30	Postdietary	1.0	0.44	1.0	175,000	29	0.45

Vitamin D Deficiency.—The rôle of the calcium ion concentration in the clotting mechanism has led to investigations involving both vitamin D and ultraviolet irradiation since the specific relation to calcium metabolism has been established. Dragstedt [3] observed a prolonged clotting time in parathyroid tetany. We have never observed bleeding disturbances in infants with tetany of rachitic origin, although the calcium level has been reduced as low as 3 mg. per hundred cubic centimeters. Dragstedt's observations refer to postoperative parathyroidectomized animals and not to infantile tetany.

Brougher [4] brought the clotting time in dogs with parathyroid tetany to normal by the administration of cod liver oil. Seyle [5] recorded the acceleration of the clotting time in several patients after the use of viosterol. The finding of a normal clotting time in patients with syphilis or obstructive jaundice within four hours after the administration of viosterol does not necessarily mean that bleeding

3. Dragstedt, L. R., and Sudan, A. C.: Am. J. Physiol. **35**:225, 1926.
4. Brougher, J. C.: Am. J. Physiol. **37**:221, 1928.
5. Seyle, H.: Klin. Wchnschr. **7**:1891, 1928.

from the tissues has been arrested. A normal clotting time is no safeguard against bleeding from vascular injury due to infectious processes.

Ultraviolet irradiation has been observed to produce varying effects on the animal body, particularly in relation to the clotting mechanism. Levi [6] demonstrated increased capillary permeability to red cells on exposure to ultraviolet rays, in the nature of a diapedesis.[7] Leonard Hill made the pertinent observation during the war that in soldiers tramping for prolonged periods under constant exposure to the sun bleeding from the mucous membranes occurred more readily than in those who kept in the shade. This was brought to the attention of the medical officers by the dental services of the allied forces. Hausmann [8] later observed clinically that excessive exposure to ultraviolet irradiation was more conducive to hemorrhage in tuberculous patients than in a control series.

Sanford [9] found that brief exposure to ultraviolet irradiation shortens the bleeding time of new-born infants but does not affect the coagulation time. She found a rise in the number of platelets during the course of the exposure but a return to normal when ultraviolet irradiation was discontinued. Sooy [10] observed a rise in the number of platelets in a case of thrombopenic purpura in an adult after daily exposure to ultraviolet irradiation. But Ceruti [11] observed that irradiation with ultraviolet rays for ten minutes reduced the coagulation time by one-half in some cases and prolonged it in others. Gunn [12] found that by exposing young rabbits to irradiation from the mercury lamp, a distinct increase in the number of thrombocytes was obtained in a week. Phillips [13] further observed that viosterol increases the thrombocytes and shortens the clotting time in normal animals.

A vitamin D deficient dietary consisted of 76 per cent yellow corn, 20 per cent wheat gluten, 3 per cent calcium carbonate and 1 per cent sodium chloride, according to Steinbock. After the diet had been maintained for four weeks, rachitic manifestations were confirmed clinically, roentgenologically and by the changes in the calcium and phosphate content of the blood. The rats so maintained showed diffi-

6. Levi, M.: Strahlentherapie **7**:602, 1916.

7. This footnote was deleted by the author.

8. Hausmann, W.: Grundzüge der Lichtbiology und Lichtpathologie, Berlin, Urban & Schwarzenberg, 1923.

9. Sanford, H. N.: Effect of Ultraviolet Light on the Blood of New-Born Infants, Am. J. Dis. Child. **33**:50 (Jan.) 1927.

10. Sooy, J. W., and Moise, T. S.: Treatment of Idiopathic Purpura Hemorrhagica, J. A. M. A. **87**:94 (July 10) 1926.

11. Ceruti, G.: Minerva med. **10**:41, 1930.

12. Gunn, F. D.: Proc. Soc. Exper. Biol. & Med. **24**:120, 1926.

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culty in using their hind legs, and the gait was shambling; the weight was practically stationary. The roentgenogram showed broad bands of uncalcified cartilage in the ends of the tibia and femur, and the blood phosphate was reduced.

Vitamin D deprivation produces a moderate diminution in the prothrombin and fibrinogen content of the blood and only slight alteration in the platelet count. The reduction in the blood clotting index parallels the striking diminution in prothrombin and fibrinogen, substances associated with the plasma protein level of the blood. The relatively slight alteration in the platelet level when the dietary is deficient in vitamin D throws some doubt on the direct relationship of vitamin D per se to platelet formation. Previous observers have been able to stimulate bone marrow temporarily by vitamin D or its equivalents and thus to obtain an increased platelet count. While these

TABLE 4.—*Vitamin D Deficiency*

Date	Determination	Prothrombin	Fibrinogen	Antithrombin	Platelets		Index
					Concentration	Lysis, per Cent	
9/18/30	Predietary	0.92	0.42	1.0	605,000	42	0.4
12/25/30	Postdietary	0.75	0.24	1.18	510,000	41	0.15
10/28/30	Predietary	1.0	0.5	1.0	580,000	45	0.45
11/20/30	Postdietary	0.72	0.28	1.0	500,000	45	0.25

procedures are suggestive, they are not conclusive, because deprivation of vitamin D produces little diminution in the platelet count.

CONCLUSIONS

1. Deficiency in vitamins in the daily dietary produces in the clotting mechanism a tendency toward potential bleeding, without actually inducing bleeding. This alteration in the clotting mechanism is generally the result of nutritional dystrophy rather than of specific vitamin deficiency.

2. Vitamin A deprivation produces a gradual diminution in the fibrinogen content of the blood paralleling the duration of the deficiency without affecting the platelet level.

3. Vitamin B deprivation produces a slight diminution in the fibrinogen content of the blood.

4. Vitamin C deprivation produces no change in the clotting components of the blood.

5. Vitamin D deprivation diminishes the prothrombin and fibrinogen content of the blood, without appreciable change in the platelet concentration.

THE SUBSTANCES INVOLVED IN THE COAGULATION OF THE BLOOD OF THE NEW-BORN *

HEYWORTH N. SANFORD, M.D.

T. H. GASTEYER, M.D.

AND

LOIS WYAT, S.B.

CHICAGO

The coagulation of blood is such a prominent phenomenon that it has attracted attention at all times, and as a result numerous theories to account for it have been advanced. In recent years much experimental work has been done on the subject, the results of which have changed many of the former conceptions. In the blood of young organisms there is a tissue that is comparatively new in its body function and as yet has not been acted on by many external conditions. For this reason the substances involved in the coagulation of the blood of the new-born infant were studied.

The first study was based on a series of thirty-five new-born infants. The mothers had been under the care of the obstetric department and were on a standard diet [1] during the prenatal period. The infants were fed regularly at four hour intervals, being sent to breast at the first regular interval after delivery; then the breast milk was supplemented at each feeding thereafter with a mixture of two-thirds milk, one-third water and 6 per cent dextrimaltose, beginning with ½ ounce and increasing by ½ ounce a day until 3 ounces was given. The infants were all of normal delivery, and the mothers had not been subjected to any anesthetic that would interfere with the bleeding and coagulation time.[2] Each infant was given a thorough examination every day, and no infants were used who showed any gross physical changes or any deviation from the normal. No infants were included in this series from whom blood was not taken for ten consecutive days.

* Submitted for publication, April 21, 1931.

* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital.

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2. Sanford, H. N.: The Effect of the Gas Anesthetics Used in Labor on the Bleeding and Coagulation Time of the New-Born, J. A. M. A. **86**:265 (Jan. 23) 1926.

METHOD

Four cubic centimeters of venous blood was used in these determinations, 1 cc. being placed in each of three dry sterile microtest tubes. The remainder was used to test the clotting time and platelets. This blood was drawn as soon after birth as practical and at daily intervals thereafter, at the same time each day.

The clotting time, bleeding time and blood platelets were estimated by slight modifications of the methods of Rudolf,[3] Duke,[4] and Rees and Echer[5] as has been described by Sanford.[6]

Prothrombin Index.[7]—One cubic centimeter of the new-born infant's blood was placed in a microtest tube containing 0.1 cc. of 1 per cent sodium oxalate solution and centrifugated. One-tenth cubic centimeter of the resulting plasma was placed in three tubes in a water bath at 38 C., and to these were added in series 0.1, 0.2 and 0.3 cc. of a 0.5 per cent solution of calcium chloride ($CaCl_2$ 6 H_2O). The shortest clotting time in the series is the prothrombin time. The prothrombin index is the ratio of the clotting time of the control blood to that of the patient's blood, or P : C = P.I.

Antithrombin Index.[8]—One cubic centimeter of the new-born infant's blood was placed in a microtest tube and centrifugated. One-tenth cubic centimeter of the resultant serum was pipetted into a microtest tube and heated in a water bath at 60 C. for ten minutes to destroy the prothrombin. A control blood was carried through the same procedure. The heated serums were cooled and to each was added 0.3 cc. of a prepared solution of thrombin (described later). The tubes were then placed in a water bath at 38 C. The antithrombin index is the ratio of the clotting time of the patient's blood to that of the control, C : P = A.T.

Fibrinogen and thrombin were prepared by drawing 50 cc. of normal adult whole blood into a vessel containing sufficient sodium citrate to give a final concentration of 0.5 per cent. To each 25 cc. of the plasma collected by centrifugating was added 4 Gm. of sodium chloride. The precipitated fibrinogen was collected, washed several times in 15 per cent sodium chloride containing 0.5 per cent sodium citrate and finally dissolved in 25 cc. of 0.5 per cent sodium citrate.

The thrombin was prepared by taking 25 cc. of the plasma collected by the procedure described, and precipitating it by 10 Gm. of ammonium sulphate. The precipitate was filtered out by means of a Buchner funnel to obviate dialysis. This precipitate containing the plasma prothrombin may be preserved for weeks as a moist paste. The thrombin solution is prepared by dissolving 0.25 Gm. of the paste in 10 cc. of water, adding 2 cc. of 0.1 per cent emulsion of cephalin and 2 cc. of 1 per cent solution of $CaCl_2$ 6 H_2O. This thrombin solution remains active for several hours.

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6. Sanford, H. N.: The Effect of Ultraviolet Light on the Blood of the New-Born, Am. J. Dis. Child. **33**:50 (Jan.) 1927.

7. Howell, W. H.: Harvey Lecture, Philadelphia, J. B. Lippincott Company, 1917.

8. Kugelmass, I. N.: Compt. rend. Soc. de biol. **87**:802, 1922.

Fibrinogen Value.[9]—Two cubic centimeters of the new-born infant's blood was placed in a microtest tube containing 0.2 cc. of a 3.5 per cent sodium citrate solution and centrifugated. The plasma was then divided into two equal portions: to one was added 0.1 cc. of a 1.5 per cent calcium chloride solution ($CaCl_2$ 6 H_2O) to coagulate the fibrinogen. The clot was removed, and the serum withdrawn.

The refractive index of the plasma at 38 C. was estimated by means of a Zeiss refractometer. The refractive index of the serum was then determined in the same manner. The percentage of fibrinogen in the blood of the new-born infant is, therefore, the difference between the index of the plasma and that of the serum, multiplied by the factor 0.187.

Clotting Index.—Kugelmass and his co-workers [9] concisely stated that in the chemical mechanism, the activity for clotting is proportional to the concentration of each interactive substance, or prothrombin plus fibrinogen plus platelets balances antithrombin. The clotting index may, therefore, be evaluated as follows:

$$\text{Clotting Index} = \frac{\text{Prothrombin} \times \text{Fibrinogen}}{\text{Antithrombin}}$$

Average Results of Analysis of Daily Coagulation Factors in Thirty-Five Normal New-Born Infants

Age, Hrs.	Clotting Time, Mins.	Bleeding Time, Mins.	Platelets	Pro-Thrombin Index	Fibrinogen	Anti-Thrombin Index	Clotting Index
12	4.5	3.0	250,000	1.85	0.624	1.48	0.659
24	4.0	3.0	300,000	1.64	0.527	1.07	0.970
48	4.5	3.5	280,000	1.72	0.634	0.97	0.968
72	5.0	4.0	320,000	1.78	0.684	1.25	0.944
96	6.0	4.0	300,000	1.15	0.680	1.31	0.596
120	5.0	3.5	280,000	0.95	0.592	1.01	0.556
144	4.5	3.0	280,000	1.11	0.704	1.02	0.766
168	4.0	3.0	300,000	1.06	0.534	1.04	0.544
192	4.0	3.0	300,000	1.05	0.570	1.04	0.576
216	4.0	3.0	310,000	1.09	0.516	1.01	0.566
Normal adult	5.0	3.0	200,000	1.00	0.500	1.00	0.500

COMMENT

In the series, the clotting time, bleeding time and platelets show values that are quite in accordance with former studies. The prothrombin has a high value for the first four days of life, then falls to approximately adult value. The fibrinogen is higher than the adult value throughout the first ten days of life. This is more marked in the first few days, and then has a tendency to fall to the adult value. The antithrombin is also high early in life, but decreases toward adult value.

Whether we assume that the part prothrombin plays in blood coagulation is as a nucleus for the electrical condensation of the clotting components in the formation of a gel, or as an initiative of an unstable supersaturated solution, corresponding to a very dilute protoplasm, high values indicate accentuated coagulability of blood and low values indicate

9. Kugelmass, I. N.; Bancroft, F. W., and Stanley-Brown, M.: The Determination and Regulation of Blood Clotting Function in Childhood, Am. J. Dis. Child. **39**:471 (March) 1930.

a tendency to bleeding.[10] The values found for prothrombin early in life, therefore, indicate that the tendency is toward an increased blood coagulability. This tendency is also shown by the fibrinogen. Fibrinogen constitutes the potential clot structure dispersed in the plasma in the most readily precipitable form. High fibrinogen content accelerates clotting.[11]

Antithrombin maintains the stability of the plasma complex, or keeps the blood in a fluid state. When blood is shed, the dissociation of the plasma produces clotting components which decrease the stabilizing effect of the antithrombin. High values of antithrombin indicate a hemorrhagic tendency.[12] For the first few days of life the antithrombin values are higher than for the normal adult, but only in proportion with the increased fibrinogen and prothrombin values to balance the system. This system balance is shown by the clotting index which is high for the first four days of life, being almost double the normal adult value. It drops abruptly to practically normal value on the fifth day owing to a decrease of all the clotting elements. The clotting and bleeding time corresponds to the usual increase found in these values at this period.

The values of the blood clotting elements indicate that in the normal new-born infant every factor is in favor of increased coagulability under normal conditions. Other influences must be considered to cause a change in these various components if spontaneous hemorrhage results.[13]

RESULTS

1. Values of the substances involved in blood coagulation are given for thirty-five normal new-born infants.

2. The substances involved in blood coagulation are high in new-born infants for the first few days, then fall to normal adult value.

952 North Michigan Avenue.

10. Mills, C. A.: Blood Clotting Studies in Hemophilia, Am. J. Physiol. **76:** 632 (May) 1926.

11. Rosenthal, F.; Licht, H., and Melchior, E.: Weitere Untersuchungen am leberlosen Säugetier, Arch. f. exper. Path. u. Pharmakol. **115:**138, 1926.

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13. These data will be reported later.

EFFECT OF CURD TENSION ON THE DIGESTIBILITY OF MILK*

D. L. ESPE, PH.D.
AND
J. A. DYE, PH.D.
ITHACA, N. Y.

The first systematic investigation of the time required for the digestion of milk was probably made by Penzoldt and his school.[1] Epstein, Czerney and Wohlmann, pupils of Penzoldt, discovered that the normal period for the emptying of the infant's stomach after breast feeding was from one and one-half to two hours. Through experiments on artificially fed infants, these investigators found that cow's milk frequently remained in the stomach as long as three hours. They were forced to depend on the regurgitation of the milk for their data. The roentgen rays were not used until Tobler, a pupil of Peiser, accidentally discovered that digestion could be correlated with certain changes noted on the roentgenograms they were taking of hospital patients. In 1908, Tobler and Bogen [2] published a comprehensive study on the factors influencing gastric digestion of milk, as determined by roentgenograms. Their work is still the basis of many theories advanced by pediatricians.

In 1916, Allemann and Schmid [3] published an extensive study on the physical character of the curd of cow's milk, noting the influence of the following factors on curd tension: amount of rennin, temperature of coagulation and addition of ammonia, acid and calcium chloride; also individuality, period of lactation, variation from milking to milking, variation between the first and the last drawn milk and the effect of various feeds. Their method was to coagulate the milk with rennin and measure the curd tension by means of a small device consisting of con-

* Submitted for publication, April 18, 1931.

* From the Department of Physiology and Biochemistry, Cornell Medical College, Cornell University.

* The Sarah Manning Sage Research Foundation of Cornell University gave financial aid in connection with this work.

1. Penzoldt, F.: Beiträge zur Lehre von der menschlichen Magenverdauung unter normalen und abnormalen Verhältnissen, Deutsches Arch. f. klin. Med. **51:** 535, 1893.

2. Tobler, L., and Bogen, H.: Ueber die Dauer der Magenverdauung der Milch und ihre Beeinflussung durch verschiedene Factoren, nebst Beobachtungen über das Verhalten des Säuglingsmagens im Röntgen-Bild, Monatschr. f. Kinderh. **7:**12, 1908-1909.

3. Allemann, D., and Schmid, H.: Ueber die Festigkeit des durch Laberzaugten Milchkoagulums, Landwirtschaftl. Jahrb. d. Schweiz. **30:**355, 1916.

centric rings attached to a slender, upright bar. This instrument was placed in the beaker containing the sample of milk to be tested. After the formation of the clot on the addition of rennin, this curd knife was slowly drawn vertically, the curd tension being measured by the spring balance attached to the knife.

Hill,[4] in 1916, was the first to make practical use of this method in selecting milk for infant feeding. He modified the curd knives slightly by using a crow-foot arrangement with sharpened cutting edges instead of the concentric ring type of tester used by Allemann and Schmid. With this device, trained assistants made hundreds of tests of milk used for infant feeding. Almost without exception, the milk with a low curd tension was more readily digested by the infant than milk with high curd tension. Hill has done little to determine the cause of this variation in curd tension of different milks, except to show that there is some correlation between the proteins of milk and curd tension. His most recent bulletin[5] shows the effect of pasteurization on curd tension. Freudenberg[6] has probably made a more thorough study of the factors influencing the digestibility of milk for infants than any other present day pediatrician. So far as the authors have been able to ascertain, however, his methods for studying the relationship between curd tension and the digestibility of milk have not been quantitative.

EXPERIMENTAL DATA

The purpose of the experiments presented in this paper was to obtain a quantitative expression of the effect of varying curd tensions on the length of the digestive period. For this, Pavlov stomach pouches were made in dogs. Milk of varying curd tensions was fed to these animals, and the length of the digestive period was determined by the secretion period and by analysis of the gastric juice obtained from these pouches. In addition to measuring the amount of gastric juice secreted, the free and combined acid, the p_H and the peptic activity were also determined. Topfer's reagent and phenolphthalein were used in calculating the free and combined acid. The hydrogen ion concentration was measured electrometrically, while the peptic activity was determined by the formaldehyde titration method, purified albumin being used as a substrate. It was found, however, that the quantity of gastric juice secreted by the pouch was the best index of the course of digestion of the food in the main part of the stomach. The continuous flow of gastric juice secreted by the pouch was collected throughout the total digestive period.

Since the fat content of cow's milk varies considerably for the various breeds of dairy cattle and to some extent from animal to animal within a single

4. Hill, R. L.: The Physical Curd Character of Milk and Its Relationship to the Digestibility and Food Value of Milk for Infants, Utah Agr. Exper. Sta. Bull. 207 (June) 1928.

5. Hill, R. L.: Utah Agr. Exper. Sta. Bull. 227 (June) 1931.

6. Freudenberg, E.: Physiologie und Pathologie der Verdauung im Säuglingsalter, Berlin, Julius Springer, 1929.

breed, the milk used in these trials was separated immediately after milking. This removed the most obvious variable. Aliquot samples were then used for analyses and digestion tests. These analyses included determination of curd tension and percentage of casein, total protein, solids not fat, ash and p_H. Curd tension was measured by the Hill modification of the Allemann and Schmid method. However, the knives were made somewhat larger than those used by Hill and with extremely sharp blades. These mechanical differences make comparison of the data on curd tension here presented with those of other workers only relative. The Kjeldahl method was employed for the nitrogen determinations. All analyses were run in duplicate. Milk from a single cow was then used for all trials requiring the same curd tension. To secure milk of varying curd tensions, the milk from cows of different breeds was obtained. A few digestibility tests were made on calves by means of roentgenograms for both soft and hard-curded milks. Similar observations were made on man through the use of the fluoroscopic screen. The results of these trials have been compiled in table 1.

TABLE 1.—*Influence of Curd Tension on the Digestibility of Milk*

Animals	No. of Trials	Curd Tension of Milk Fed, Gm.	Amount Fed, Cc.	Length of Digestive Period, Hr.	Method of Determining Length of Digestive Period
Dog 3.....	12	98	300*	1.8	Secretion from Pavlov pouch
	7	139	300	2.0	Secretion from Pavlov pouch
	6	174	300	2.2	Secretion from Pavlov pouch
	9	190	300	2.3	Secretion from Pavlov pouch
Dog 4.....	12	98	500	1.7	Secretion from Pavlov pouch
	6	139	500	2.0	Secretion from Pavlov pouch
	13	174	500	2.8	Secretion from Pavlov pouch
	5	190	500	2.8	Secretion from Pavlov pouch
Calf 4.....	1	66	946†	4.0	Roentgenograms
	1	141	946	6.0	Roentgenograms
Man.....	1	98	300	1.75	Fluoroscopic screen
	1	190	300	2.75	Fluoroscopic screen

* Each dog was fed a test meal of approximately one-half the amount of milk that it would normally consume after fasting for twelve hours.
† One quart plus 100 Gm. of barium sulphate.

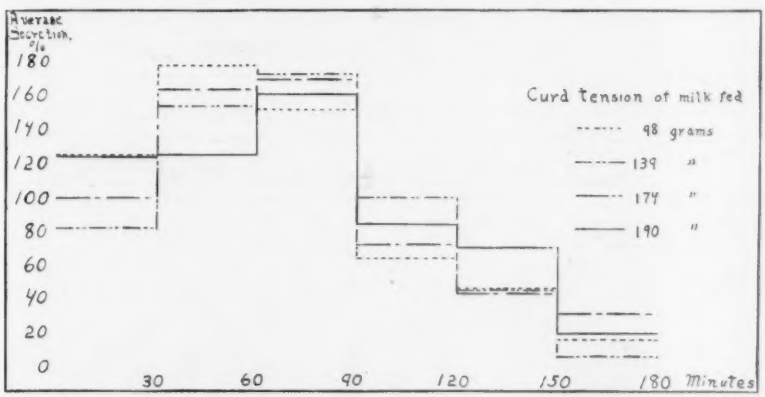
RESULTS

An adult dog requires from 1.7 to 1.8 hours to digest milk of low curd tension, namely 98 Gm., while milk having a relatively tough curd, 190 Gm., remains in the stomach of the same animal from 2.3 to 2.8 hours. The variations in rate of digestion from animal to animal may be due to individuality or to changing environmental conditions at the time, such as weather or local disturbing factors. More recent work has shown that the length of the digestion period for calves may be considerably longer than that indicated here.

The rate of secretion was not influenced by the curd tension of the milk, as shown by the accompanying graph. Though the average percent of secretion in each half hour period varied for milk of varying curd tensions, no correlation exists between these various levels of gastric secretion. Again, it seems that individuality is of major importance

in interpreting this variation. However, the persistency of secretion does respond to the toughness of the milk curd. This is not true of the other factors measured (free and combined acid, p_H and peptic activity), as shown by table 2.

The slight decrease in free acid at first might be explained by a more constant though relatively much smaller secretion of mucus than of gas-



Effect of the curd tension of milk on the rate of gastric secretion.

TABLE 2.—*Effect of Curd Tension of Milk on Gastric Secretion*

	Milk of 98 Gm. Curd Tension (12 Trials)					
	30 Min.	60 Min.	90 Min.	120 Min.	150 Min.	180 Min.
Free acid	9.00	10.69	10.84	10.44	9.59	9.05
Combined acid	1.53	1.69	1.55	1.71	1.83	1.85
Total acid	10.53	12.38	12.39	12.15	11.42	10.90
p_H	1.18	1.10	1.13	1.17	1.14	
Peptic activity	3.32	3.01	2.98	3.18	2.97	3.24
Volume	7.89	15.84	11.72	5.24	3.04	2.31
	Milk of 190 Gm. Curd Tension (3 Trials)					
	30 Min.	60 Min.	90 Min.	120 Min.	150 Min.	180 Min.
Free acid	7.87	9.98	10.75	10.83	10.43	10.03
Combined acid	1.68	1.30	1.17	1.28	1.42	1.63
Total acid	9.55	11.28	11.92	12.11	11.85	11.66
p_H	1.22	1.10	1.10	1.10	1.14	1.15
Peptic activity	3.13	2.73	2.78	2.95	2.55	2.50
Volume	6.67	9.77	10.30	5.17	2.50	1.30

tric juice by the pouch. As the rate of gastric secretion increases, the alkaline mucus is neutralized without as great a change in p_H as when the mucus is proportionately greater.

Tobler and Bogen have determined the effect of diluting milk for infant feeding on the length of the digestive period. Calculation of the curd tension for these dilutions gave the results tabulated in table 3.

These data show that diluting milk to secure a lower curd tension, without decreasing the amount of milk fed, does not shorten the length of the digestive period. It appears that diluted milk has a different

physiologic action on the dog's than on the child's stomach. Certainly, curd tension is not the only factor in determining the digestibility of prepared infant foods.

That curd tension is not directly proportional to the concentration of any of the milk constituents seems evident. In table 4, the actual curd tension of milk diluted in varying ratios is compared with the theoretical curd tension if dilution were the only factor involved.

There is, however, a marked correlation between curd tension and certain of the constituents of milk, particularly the proteins. This is

TABLE 3.—*Influence of the Dilution of Milk on Its Curd Tension and Digestibility*

	Total Volume, Cc.	Milk, Cc.	Water, Cc.	Ratio of Milk to Water	Curd Tension	Time of Digestion, Min.
Dog	300	100	200	1:2	1	220
	300	150	150	1:1	26	265
	300	200	100	2:1	51	320
Child (3 months old)	90	30	60	1:2	1	55
	90	45	45	1:1	26	85
	90	60	30	2:1	51	103
Dog	100	100	0	1:0	117	190
	200	100	100	1:1	26	220
	300	100	200	1:2	1	185
	400	100	300	1:3	0	165
Child (3½ months old)	50	50	0	1:0	117	55
	100	50	50	1:1	26	65
	150	50	100	1:2	1	105

TABLE 4.—*The Influence of Dilution on Curd Tension*

Dilution (Milk to Water)	Actual Curd Tension	Theoretical Curd Tension	p_H
1:0	117	117*	6.63
4:1	71	94	
3:1	68	88	
2:1	51	78	
3:2	46	71	
1:1	26	59	6.7
1:2	1	39	
1:3	0 (would hardly support clot)	29	
1:4	0 (would not support clot)	23	6.8

* This figure was obtained by calculating the theoretical effect of the dilution of milk with water in the ratios given.

shown in the analyses given in table 5. As the correlation of casein, or even total protein, and curd tension is far from unity (coefficient of correlation of curd tension and casein, 0.895 ± 0.045; curd tension and protein, 0.880 ± 0.051; curd tension and solids, 0.941 ± 0.029; curd tension and ash, 0.613 ± 0.208, and curd tension and p_H, -0.457 ± 0.188), other factors must have a modifying influence. For instance, in two samples of milk with 2.11 per cent and 2.82 per cent of casein, respectively, the difference in casein content accounted for only 51 per cent of the actual difference in curd tension; in other words, the curd tension of the respective samples was 113.5 and 188.25 Gm. If the correlation

between casein and curd tension had been unity in this instance, an increase of casein from 2.11 to 2.82 per cent would account for an increase of curd tension only from 113.5 to 151.7 Gm.

The hydrogen ion concentration of the milk before coagulation was found to be one of the modifying factors just referred to, as shown by table 6. However, various samples of normal sweet milk varied only about two tenths of a p_H in reaction, too small an amount to affect curd tension noticeably.

Another factor that greatly influences curd tension is the boiling of milk. A sample of raw milk of 117 Gm. curd tension when boiled had a curd tension of 5 Gm. This indicates that the proteins are of primary

TABLE 5.—*Influence of the Composition of Milk on Its Curd Tension*

Sample	Curd Tension	Per Cent of Casein	Per Cent of Protein	Per Cent of Solids	Per Cent of Ash	p_H
1	182	2.69	3.39	10.04	0.781	6.65
2	197	3.22	4.04	10.55	0.893	6.65
3	192	2.93	3.75	.....	0.850	....
4	192	2.92	3.73	10.33	0.566	....
5	55	1.61	2.21	8.45	0.436	6.80
6	84	1.95	2.91	9.35	0.534	6.80
7	94	1.94	2.90	.....	0.786	6.78
8	117	....	....	9.42	0.769	6.60
9	139	2.54	3.13	9.31	0.845	6.65
10	174	3.10	3.80	10.39	0.902	6.65
11	100	2.68	3.59	.....	.....	6.73

TABLE 6.—*Influence of p_H on the Curd Tension of Milk*

Amount of 10 per Cent Acetic Acid Added, Cc.	Curd Tension	p_H
0.0	117	6.63
0.5	142	
1.0	164	6.15
1.5	192	5.90
2.0	(Too tough to measure)	

importance in determining the curd tension of milk, for boiling denatures them. The modifying action of certain materials on curd tension, such as sodium citrate, calcium chloride, hirudin, etc., may be due to the formation of a different chemical compound or to adsorption compounds with casein. It is quite possible that a soluble paracaseinate is formed when sodium citrate is added. When calcium chloride is added, the hydrogen ion concentration may be partially responsible for the increased curd tension. That the colloidal calcium phosphate has little influence on curd tension seems likely from the following indirect tests. Van Slyke and Bosworth [7] have shown that three fourths of the colloidal calcium phosphate may be removed by centrifugating milk at high speed

7. Van Slyke, L. L., and Bosworth, A. W.: Condition of Casein and Salts in Milk, J. Biol. Chem. **20**:146, 1915.

for two hours. The curd tension of a sample of milk treated in this manner for one hour and ten minutes by us was not affected. When a large amount of milk was run through a cream separator twenty times, however, the curd tension was reduced from 85 to 80 Gm. This may have been due to a partial denaturation of the proteins as the result of foaming. On analyzing the separator slime, we found that the ratio of calcium present in the slime to that in milk, when both were calculated on the same solids basis, was as 1,500 is to 80. A modification of the Clark-Collip method [8] of calcium determination was used.

Another method of attempting to lower the percentage of colloidal calcium phosphate was to dilute the milk with water and compare this

TABLE 7.—*Influence of Calcium Chloride and Sodium Citrate on Curd Tension*

Sample	Method of Treatment	Curd Tension	p_H
1	Untreated	192	
1	5 cc. of 10% calcium chloride added	212	
1	5 cc. of 10% sodium citrate added	149	
2	Untreated	102	6.57
2	5 cc. of 10% calcium chloride added	126	6.15
2	5 cc. of 10% sodium citrate added	57	6.68
2	10 cc. of 10% sodium citrate added	(No coagulation)	6.80
3	Untreated	82	
3	5 cc. of 10% calcium chloride added	83	
3	5 cc. of 10% sodium citrate added	70	

TABLE 8.—*Influence of Albumin and Cream on the Curd Tension of Milk*

Sample	Method of Treatment	Curd Tension
1	Untreated	86
	50 cc. of 40% cream added	78
2	Untreated	104
	10 cc. of 4.46% albumin added	105
3	Untreated	192
	25 cc. of 35% cream added	186

with aliquot samples of milk diluted with its own whey obtained by coagulating part of the milk with rennin. The whey was then added with the rennin used in coagulating the sample of milk prior to testing. The difference in curd tension between milk diluted with water and milk diluted with whey was within the range of experimental error. This evidence does not indicate that the mineral matter in milk is without effect on curd tension. For instance, we know that the removal of the soluble calcium of milk prevents coagulation. The addition of small amounts of calcium chloride or sodium citrate also markedly influences curd tension, as shown in table 7. An explanation of the cause of this variation in curd tension will not be attempted at this time.

8. Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Company, 1927, p. 408.

That "protective" substances, such as fat and soluble proteins, do not influence curd tension greatly is shown in table 8. Two hundred and fifty cubic centimeter samples were used in these trials.

COMMENT

Milk, entering the stomach as a liquid, is changed to a solid on coagulation. After coagulation has occurred, digestion, as has been frequently shown by Brennemann and others, is a peripheral process. Any factor that tends to make the digesting mass more porous—to lower curd tension—or cause it to absorb gastric juice more rapidly, followed by peptonization and disintegration or liquefaction, shortens the digestive period. The increased digestibility of boiled milk for infant feeding, as found by Brennemann,[9] seems to be readily explained on the basis of curd tension. As the percentage of casein of cow's milk tends to drop during the first four weeks after freshening and then to remain comparatively constant until the latter part of the next period of pregnancy, when it rises rapidly, the curd tension probably follows a somewhat parallel curve. That the usual variation in concentration in the inorganic constituents of milk has little effect on curd tension may be due to their presence in excess. Though it is readily possible to influence curd tension artificially, e. g., by adding acid, drugs or other compounds, their effect on the digestion of the curd is not known. A study of these factors will be made later.

SUMMARY

Doubling the curd tension of milk increases the length of the digestive period from 30 to 65 per cent. A normal milk of high curd tension usually means a more concentrated milk than one of low curd tension, and therefore one of greater food value.

The percentage of casein in the milk seems to be the greatest factor influencing curd tension. However, the variation in the percentage of casein accounts for only about 81 per cent of the change in curd tension. The disparagement between soluble proteins and curd tension is even greater.

Boiling markedly lowers the curd tension of milk.

Acidifying the milk before its coagulation with rennin has the opposite effect. It raises the curd tension.

The addition of small amounts of various substances, such as calcium chloride and sodium citrate, also has a marked effect on curd tension.

Diluting milk with water has the same effect on curd tension as diluting it with its own whey. However, dilution has a greater influence than merely producing a less concentrated mixture.

9. Brennemann, J.: The Curd and the Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 2) 1929.

BACILLUS MUCOSUS INFECTION OF THE NEW-BORN *

MARK JAMPOLIS, M.D.

KATHARINE M. HOWELL, M.D.

JOSEPH K. CALVIN, M.D.

AND

M. L. LEVENTHAL, M.D.

CHICAGO

I. CLINICAL REPORT

An outbreak of infectious diarrhea of unusual bacterial origin had its inception during the months of February and March of 1930 in the nursery for the new-born of the Michael Reese Hospital. Only three severe cases developed during this period, but early in April the disease began to spread rapidly, and a serious situation ensued which lasted until the middle of June.

The diarrhea in itself was not alarming, but the associated constitutional manifestations were extremely severe. The infants presented a picture resembling the "alimentary intoxication" of Finkelstein. Dehydration, stupor, icterus, pallor, toxic facial expression and a temperature ranging from 99 to 103 F. were prominent symptoms. The majority of the babies did not have respiratory complications, but in a few otitis media developed late in the course of the disease and in a small number terminal bronchopneumonia. The response to treatment was unsatisfactory, as evidenced by the high mortality.

An occasional case of diarrhea in a nursery causes no great alarm. Likewise, during the winter months, when respiratory diseases are raging, one is not surprised when a small outbreak of diarrhea occurs, for it is usually easy to account for the condition on the basis of parenteral infection. It seems strange, but it is true, that the pediatrician of today seldom attributes an attack of diarrhea to an actual inflammatory process in the intestinal canal, unless blood or pus is visible in the stool. A physician practicing among children is familiar with the tendency shown in the literature to overlook the intestines and to search for the etiologic factor in regions of the body far removed from the digestive tract.

* Submitted for publication, April 20, 1931.

* From the Departments of Pediatrics, Obstetrics and Bacteriology of the Michael Reese Hospital; aided by a grant from the Albert Kuppenheimer Fund.

In the series of cases that we are reporting we did not realize during February and March that an outbreak of infectious diarrhea was impending. Nevertheless, the feedings given to several of the sick babies, as well as the stools, were cultured many times. In April, when the diarrhea began to assume greater proportions, extensive studies were made to determine the etiologic factor. Not only were the offending micro-organisms disclosed, but they were definitely traced to carriers. When the carriers were removed from the nursery, our troubles were at an end.

CASE HISTORIES

CASE 1.—An infant delivered normally, born on Feb. 3, 1930, weighing 2,740 Gm., was placed in the private nursery. Diarrhea developed on February 12, and the baby was transferred to the pediatric department four days later, weighing 2,175 Gm. The temperature varied between 100 and 100.6 F., and there were approximately eight green, watery stools daily. The diarrhea continued, associated with vomiting, until February 25, when death occurred. Permission for autopsy was not obtained.

CASE 2.—An infant, born on Jan. 5, 1930, was fed on one-half cow's milk with 3 per cent dextri-maltose in the private nursery for five weeks, during which time pneumonia developed in the mother, with subsequent empyema, and she was transferred from the maternity division. On February 13 the baby had a temperature of 99.8 F. and had numerous, copious green stools, associated with marked loss of weight. On February 16, the infant was transferred to the pediatric department, where the diarrhea continued, associated with loss of weight, intoxication and dehydration until February 24, when death occurred, with signs of a terminal bronchopneumonia. Direct smears and cultures of the stools revealed Bacillus mucosus, B. bifidus, Micrococcus ovalis, B. coli and Staphylococcus.

CASE 3.—An infant delivered by cesarean section, born on March 10, 1930, weighing 2,765 Gm., was placed in the private nursery. Seven days later, diarrhea developed, with from six to eight green, watery stools daily. On March 19, two days later, the baby was admitted to the pediatric department, appearing quite toxic. The temperature varied between 98 and 99 F., and in spite of treatment the condition became progressively worse until death on March 27. There were signs of a terminal bronchopneumonia, and the weight immediately preceding death was 2,150 Gm.

During these two months several other cases of diarrhea occurred, but they were not as severe as the three aforementioned cases.

CASE 4.—An infant, delivered by cesarean section on April 6, 1930, following a long labor, whose birth weight was 2,815 Gm., was placed in the private nursery. Diarrhea developed on April 12, and on April 15 the baby, weighing 2,340 Gm., was admitted to the pediatric department. The stools were greenish-yellow with many curds; they numbered from six to eight daily. The child appeared stuporous. Spinal puncture performed on April 17 revealed xanthochromic fluid, but there were no signs of disease of the central nervous system. Stupor and diarrhea continued until death on April 21. Cultures of the stool revealed B. coli and a predominance of B. bifidus.

CASE 5.—An infant, one of twins, born normally on April 7, 1930, weighing 2,400 Gm., was placed in the private nursery. Diarrhea developed seven days later, and on April 19 the baby was transferred to the premature station in poor

condition. The stools were watery and numbered from four to five daily. The child appeared dehydrated and stuporous, and the diarrhea continued unaffected by treatment, until death occurred on April 26. Cultures of the stools revealed Streptococcus mitis, B. mucosus and B. coli. Autopsy revealed a subacute enteritis, with hyperplasia of the mesenteric lymph nodes. The twin progressed normally.

At this time we realized that a serious outbreak of diarrhea was beginning.

Case 6.—An infant, born normally on April 19, weighing 2,210 Gm., was transferred immediately to the pediatric department because of prematurity. Coincidentally, on the same day the baby in case 5 was transferred to the pediatric department, but to the isolation room of the premature station. Diarrhea, consisting of from three to five watery yellow stools daily, developed five days later. On May 13, the baby died, with a bilateral otitis media and bronchopneumonia. Autopsy confirmed the clinical diagnosis. The condition was considered diarrhea of parenteral origin.

Case 7.—An infant, born on April 12, 1930, after induced labor, weighing 3,285 Gm., was placed in the private nursery. Four days later, diarrhea, consisting of from six to eight watery, greenish-yellow stools, developed, and the baby was placed in isolation immediately with a special nurse in charge. In this connection, it is interesting to note that the diarrhea developed on the day after the infant in case 4 was removed from the nursery. Cultures of the stool showed Strep. mitis and B. mucosus, as did those in case 5. The diarrhea continued for several days; emaciation and dehydration followed, and death was predicted by the attending staff. However, the infant recovered and was sent home in good condition. After discharge, suppurative otitis media ensued; the pus contained staphylococci. Later impetigo spread over the face and head, and smears from the lesions also revealed staphylococci. The infant made a complete recovery.

Case 8.—A premature infant, born on April 8, 1930, weighing 2,400 Gm., was placed in the ward nursery, then transferred to the premature station on April 10, and discharged in good condition two weeks later. On April 28, the infant was readmitted to the premature station because of diarrhea, intoxication and dehydration. The diarrhea and toxic symptoms disappeared promptly, and the baby was discharged cured two weeks later. Cultures of the stool revealed B. mucosus predominating, with a few Streptococci hemolytici.

Case 9.—A well developed infant, born on April 9, 1930, by forceps delivery and placed in the private nursery, was discharged in good condition ten days later. After one day at home, diarrhea began, and on April 24 the child was readmitted to the pediatric department. The stools were numerous, about ten daily, and the baby became toxic and dehydrated. Cultures of the stool revealed a streptococcus and B. mucosus. Death occurred on April 28. Permission for autopsy was not granted.

Case 10.—An infant, born by normal delivery on April 11, 1930, was placed in the ward nursery, where it soon developed a diarrhea which was not severe. There was no intoxication, and recovery was prompt. Cultures of the stool revealed B. mucosus, B. coli and a streptococcus.

Case 11.—An infant, born by cesarean section, on May 10, 1930, weighing 3,780 Gm., was placed in the private nursery. The feedings consisted of breast milk entirely; diarrhea developed on May 24, with from eight to thirteen greenish, watery stools daily. On May 26, the infant was transferred to the pediatric department. The course of the diarrhea was then marked by remissions, with

gain in weight, alternating with marked diarrhea and loss in weight, until June 10, when the baby became cyanotic; it died on June 12, with signs of a terminal bronchopneumonia. Cultures of the stool showed B. mucosus predominating and large streptococcus. Autopsy revealed an acute ulcerative enteritis and bronchopneumonia. Cultures from the ulcerations in the intestine revealed B. mucosus in pure growth.

CASE 12.—An infant, born on May 14, 1930, normally, with a birth weight of 3,490 Gm., was given breast milk plus artificial feeding. Diarrhea began on May 18, with numerous watery stools, and the baby was transferred to the pediatric department on May 22, weighing 2,740 Gm. The temperature varied between 97 and 99 F. Cultures of the stool revealed B. mucosus, B. coli, B. bifidus and Streptococcus. Death occurred on May 23, with signs of terminal bronchopneumonia. The two days preceding death were characterized by much vomiting and jaundice. Autopsy revealed acute enteritis, bilateral bronchopneumonia and uric acid infarcts of the kidney. Cultures of the intestine revealed the same organisms found in the stool.

CASE 13.—An infant born on May 16, 1930, by low forceps delivery, weighing 2,990 Gm., was fed breast milk plus a cow's milk mixture. Diarrhea of from three to six soft green stools daily developed on May 19, and the baby was transferred to the pediatric department on May 23, weighing 2,600 Gm. and displaying signs of profound toxicity and dehydration. The stools increased in number to from ten to twelve daily, and the infant died on June 3. Culture of the stool showed B. mucosus predominating, with M. ovalus, B. coli and yeasts. Permission for autopsy was not obtained.

CASE 14.—An infant, born on May 18, 1930, weighing 2,800 Gm., was placed in the private nursery. Diarrhea began on May 21, with from two to five stools daily, and was associated with marked loss in weight and signs of dehydration. The baby was transferred to the premature station on May 28, weighing 1,800 Gm. Death occurred on May 30. Autopsy was not obtained.

CASE 15.—An infant, delivered normally on May 21, 1930, was fed both breast and cow's milk. Diarrhea began on May 24, with from two to five greenish-yellow stools daily. The diarrhea soon ceased, and the baby gained weight for a few days, but the symptoms recurred. On May 29, the infant was transferred to the pediatric department. From then on the course was rapidly fatal, death occurring on June 3. Cultures of the stool revealed B. mucosus and B. coli. Autopsy disclosed acute pyelitis and thrombosis of the inferior vena cava and of the renal and suprarenal veins. Cultures from the intestine revealed B. mucosus, with a streptococcus. A culture of the heart's blood revealed a streptococcus and B. coli.

CASE 16.—An infant was born normally on May 19, 1930, weighing 3,030 Gm. The feedings consisted of breast milk and cow's milk. Diarrhea developed on May 26, with from five to six soft, greenish, watery stools daily. The infant was transferred to the pediatric department on May 29, weighing 2,600 Gm. The temperature varied between 98.6 and 99 F. Cultures of the stool revealed B. mucosus predominating, a streptococcus and B. coli. Symptoms were severe, but the baby made a gradual and complete recovery and was discharged from the hospital cured.

CASE 17.—An infant, weighing 3,430 Gm., was born normally and spontaneously on May 17, 1930. It received breast and artificial feeding. Diarrhea developed on May 30, and the baby was transferred to the pediatric department

on the same day, weighing 3,250 Gm. The diarrhea became severe, with from eight to ten greenish, watery stools daily, and cultures of the stool revealed B. mucosus, a streptococcus and B. proteus. The temperature varied from 98.6 to 102.6 F. The symptoms were quite severe, but the baby recovered and was discharged from the hospital in good condition.

CASE 18.—An infant, born by forceps delivery on May 24, 1930, weighing 3,330 Gm., was fed with a mixture of breast milk and cow's milk. Diarrhea developed on May 28, with from five to six yellow, watery stools daily. Cultures of the stool revealed a predominance of B. mucosus, with B. coli and a streptococcus as accompanying organisms. The temperature varied between 99 and 101 F. Dehydration was extreme, and death occurred on June 6, precipitated by bronchopneumonia. Autopsy revealed acute catarrhal enteritis and confluent bronchopneumonia. Cultures of the intestinal contents revealed B. mucosus predominating and B. coli. Necropsy cultures of the heart's blood and the pleural and peritoneal fluids, and cultures of the tissues of other organs revealed B. mucosus, B. coli and Streptococcus.

CASE 19.—In an infant, delivered on May 16, 1930, by cesarean section because of placenta praevia, whose birth weight was 2,980 Gm., diarrhea developed on June 1, with from four to six soft, yellow stools daily, cultures of which revealed B. mucosus and a streptococcus. The temperature varied from 98.6 to 100 F., and the baby was transferred to the pediatric department on June 2, weighing 2,660 Gm. Intoxication and dehydration were extreme, and the diarrhea was uncontrollable. The infant died on June 10, with signs of a terminal bronchopneumonia. Autopsy revealed acute catarrhal enteritis, confluent bronchopneumonia and bilateral otitis media. Cultures of the intestinal content revealed B. mucosus in association with a streptococcus.

CASE 20.—An infant was born on May 24, 1930, and discharged after two weeks in good condition. Two days later the baby was readmitted to the pediatric department because of diarrhea, having from two to four greenish stools daily. The child appeared extremely toxic and dehydrated. Death occurred on June 6, two days after readmission, with signs of terminal bronchopneumonia. Autopsy showed acute catarrhal enteritis and confluent bronchopneumonia, with pleuritis and bilateral purulent otitis media. Cultures from the stools and from the lungs revealed almost pure growths of B. mucosus.

CASE 21.—An infant born on June 7, 1930, normally, was placed in the ward nursery. Diarrhea began on June 9 with from four to six soft, yellowish stools daily. These stools were the only ones in our series of cases that contained blood and pus. Culture of the stool revealed B. mucosus and Streptococcus, and blood was visible macroscopically and detected chemically. Despite the hemorrhagic stools, the infant did not appear acutely ill or dehydrated, and made an uneventful recovery.

CASE 22.—An infant born spontaneously on June 1, 1930, weighing 3,400 Gm., was placed in the private nursery. The feedings were entirely from the breast. Diarrhea developed on June 4; a culture of the stool revealed B. mucosus and a streptococcus, with B. coli and yeasts. The baby was not transferred, made a spontaneous uneventful recovery and was discharged from the hospital well.

Other Cases.—The remaining twelve cases of diarrhea occurred during the subsidence of the outbreak. They were mild and were not associated with loss of weight, dehydration or signs of toxemia. Under isolation precautions in a newly established nursery for suspect cases, the babies made rapid recoveries and were all discharged in good condition.

CLINICAL ANALYSIS OF CASES

Between February 3 and June 10, 1930, diarrhea developed in thirty-four infants. In twenty-two of the thirty-four, severe symptoms developed—apathy, intoxication, icterus, a slight fever, signs of dehydration and vomiting. Fourteen of these twenty-two babies died within from five to thirteen days (average, nine and three-tenths) after the onset of the diarrhea. Diarrhea developed in the remaining twelve during the last ten days of the epidemic. These twelve babies did not appear sick. The stools, however, were watery, greenish and full of mucus and in some instances looked even worse than those in the fatal cases. However, the diarrhea promptly subsided after short periods of starvation, followed by breast milk feedings, and the babies recovered completely.

All of the cases during February and March occurred in the private nursery of the main hospital. None appeared in the general ward nursery. In April, the first three cases occurred in the private nursery. The subsequent developments occurred mostly in the ward nursery. At no time did diarrhea appear in the nursery of Meyer House, a private pavilion, one floor of which is devoted to obstetric cases. This fact is interesting, because patients at Meyer House are delivered in the same room as those in the main maternity section, and the food mixtures for the babies are prepared in the same diet kitchen.

The type of delivery was varied; most of the births were normal and spontaneous, while five were by cesarean section. The onset of the diarrhea occurred from one to twenty days after birth, the average time being between the fourth and the seventh day. The baby whose diarrhea began on the twentieth day had been home four days before it was readmitted to the hospital. The shortest time of onset was thirty-six hours after delivery, with much blood and mucus in the stool. In this case cultures and smears from the stools showed almost pure cultures of B. mucosus. This was the only instance in our series in which bloody stools occurred.

The type of feeding was apparently of no etiologic significance. The babies were affected whether they had been previously fed breast milk exclusively, mixed feedings, cow's milk mixtures or powdered lactic acid milk.

The average number of stools per day was six; the largest number in any case was twelve. The stools were yellow or greenish and watery, and contained mucus and curds. In many of the cases that developed in the latter part of the outbreak, there were formed stools at times during the diarrheal course. The appearance of the stools did not indicate the severity of the disease. Some of the sickest babies had stools of more normal appearance than those who had mild courses.

The temperature was usually low, ranging from 97.5 to 100.5 F. In a few instances, the temperature reached 103 F. In five of the severe cases urinalysis showed: albumin, 2 plus; sugar, 1 plus, many granular casts and a few red blood cells. The red blood corpuscles and hemoglobin were slightly below normal. The leukocyte count averaged about 15,000 in most cases; in one case it was as low as 9,400 and in another, as high as 52,000. A differential leukocyte count averaged 33 per cent polymorphonuclear leukocytes, 58 per cent lymphocytes and 6 per cent mononuclears.

In several of the fatal cases terminal bronchopneumonia developed and in a few, purulent otitis media. In the last two cases in which the patients died with terminal pneumonia, almost pure cultures of B. mucosus were recovered from the lungs.

TREATMENT

Treatment was apparently of little avail in the severe types of infection. In all cases the patient underwent preliminary periods of starvation, varying from twelve to thirty-six hours, although tea or Ringer's solution was given freely by mouth unless vomiting prevented. Whether the period of starvation was short or long, the signs of intoxication did not disappear. After this period, small amounts of breast milk were usually given, although occasionally lactic acid milk or protein milk was used. The infants seemed to do better when the quantity given was small at first (1 or 2 drachms [3.9 or 7.8 Gm.] every two hours, the amount being increased very slowly). The sick babies received daily indirect transfusions of blood and subcutaneous injections of dextrose or Ringer's solution. Practically all appeared moribund at the height of the disease. Those that survived apparently did so regardless of treatment.

II. BACTERIOLOGIC STUDIES

By Dr. Howell

PRELIMINARY OUTBREAK [1]

Repeated specimens of the stools from each infant were sent to the bacteriologic laboratory for examination. The stools appeared fairly normal; they were yellow and partially formed, with little mucus and no blood. Direct smear examination revealed, in varying proportion, large gram-positive bacilli, large gram-positive cocci, chains of gram-positive cocci, small gram-negative bacilli and large gram-negative encapsulated bacilli; in brief, a bacterial flora not at variance with the stool of a normal breast-fed or artificially fed infant. The stools were cultured aerobically and anaerobically in ascites dextrose broth, blood agar,

1. The preliminary and second outbreaks are reported in part I.

Endo's agar, and litmus milk. The cultures contained B. coli, B. mucosus, B. bifidus (one case), M. ovalis, and anhemolytic streptococci in considerable numbers. The streptococci were isolated and typed according to Holman's classification. The strains were as follows: Strep. nonhemolyticus II, Strep. equinis and Strep. fecalis. No bacteria of the typhoid, paratyphoid or dysentery groups occurred in any of the cultures, nor were gas bacilli, Morgan's bacillus, enterococcus or Bargen's diplococcus encountered.

Blood cultures were taken from several infants. These gave uniformly negative results.

The mortality of the infants with diarrhea was high. Autopsies on two babies were secured—both cases had developed outside the hospital. Autopsy cultures of intestinal content and from ground spleen, gallbladder, liver and intestinal mucosa yielded B. mucosus and hemolytic streptococci of various types, B. coli and occasionally B. alkaligenes. One heart's blood culture revealed Streptococcus equinus. The other heart's blood culture was negative.

From the seventh to the tenth day of the outbreak of diarrhea, an investigation was started to determine its cause. The feedings were cultured on several successive days. In a few instances the breast milk from wetnurses contained Staphylococcus albus and diphtheroids. The artificial feedings yielded B. bulgaricus and Streptococcus lacticus.

The possibility of a carrier among the persons in contact with the infants and in the diet kitchen was considered. Nasopharyngeal cultures from the contacts—doctors, nurses, nursemaids and dietitians, about fifty in all—were studied by direct smear examination and by aerobic and anaerobic cultures taken on various mediums, meat infusion, dextrose broth, blood agar and Endo's agar. The characteristic mixed nasopharyngeal flora consisted of Staphylococcus, Strep. hemolyticus and Strep. viridans, M. catarrhalis, streptobacilli, Friedländer's bacillus, B. infiuenzae, B. fusiformis, streptothrix, etc. Nasopharyngeal examinations did not yield any bacterium in approximately pure culture. Streptococci predominated in five cultures; they were not of the Streptococcus scarlatinae nor of the Streptococcus epidemicus strains.

The cultures were repeated on the patients showing the streptococcus flora, and the typical mixed flora was found, indicating that the streptococcus had been transient rather than established.

In view of the facts that no carriers were found among the contacts, that the feeding for the infants did not contain virulent organisms, that approximately as many patients with diarrhea had been admitted from outside of the hospital as from the maternity nursery, and principally, that there were no new cases of diarrhea, the investigation was discontinued.

Cultures of the pathogenic material had yielded either B. mucosus or Strep. anhemolyticus or the two organisms in conjunction. Cultures from other sources revealed on the whole a predominance of streptococcus over other organisms. At this time it was thought that possibly some feeding that had been contaminated was the source of the diarrhea. Recommendations were made with regard to special care in keeping the feedings free from bacterial contamination.

SECOND OUTBREAK: EPIDEMIOLOGY

A detailed study of the nurseries was made from a bacteriologic standpoint. Open blood-agar plates were exposed for one half hour in the various nurseries. Those from the nursery with the more acutely ill infants had a higher colony count than those from the other nurseries; for example, in the former, 300 colonies per plate were found, while the plates from the nursery in which the milder cases of diarrhea occurred showed 150 colonies, and those from the nurseries in which diarrhea was suspected and those from the nursery for the healthy infants showed less than 50 colonies per plate. The plates with the high colony count contained more pathogenic organisms, for example, B. mucosus and B. coli, together with air organisms.

Cultures of the bed linens contained a variety of organisms, including many intestinal types. Linens of one bed occasionally touched those of the next, constituting a ready means of spreading an infection. Recommendations were made that the space between beds be increased.

Cultures were made from the rubber nipples for the nursing bottles directly after they were autoclaved, with negative results. Cultures were again made after the nipples were placed on the nursing bottles containing the artificial feedings. A mixed bacterial flora resulted, air types predominating. It is interesting to note, however, that more pathogenic bacteria were obtained in the nurseries with the severely ill infants. Cultures made from the pasteboard caps on the bottles of artificial feedings were similar in nature to the cultures of rubber nipples.

Cultures were taken from the nipples of the mothers of the children in whom severe diarrhea developed and Staph. albus, streptococci, diphtheroids and air cocci were obtained. Similar cultures were obtained from a control group of mothers with healthy infants. It is interesting to note that there were no abscesses of the breast in either group of mothers.

The autoclaves throughout the hospital are tested for sterility at frequent intervals by subjecting test tubes containing B. subtilis to the temperature of the autoclaves. No growth of organisms after seventy-two hours indicates that the apparatus is producing sterility. Several tests of the autoclaves made during these epidemics indicated that they

were in perfect condition. Cultures of the water from the various sterilizers and drinking fountains are also made as a routine procedure. No increase in organisms was noted at this period; water Vibrio, the B. subtilis group and nonpathogenic cocci constituted the organisms isolated.

Cultures were taken from the doctors', nurses' and nursemaids' hands under various conditions. A large variety of organisms were isolated, including streptococci, M. ovalis, M. catarrhalis, staphylococci, large gram-positive bacilli, B. coli, B. bulgaricus, air cocci, yeasts, etc. Cultures were taken from the nursemaids' hands before and after caring for infants. In the latter instance, there was an increase in the number and variety of bacteria, many more intestinal types appearing. It was observed that nursemaids occasionally failed to wash their hands between caring for one infant and feeding another, an excellent means of propagating an infection after it has started.

The infants' milk feedings, both the constituents and the completed feeding, were cultured. The breast milk contained Staph. albus, diphtheroids and air cocci; the whole lactic acid milk, Strep. lacticus and B. bulgaricus; ward feedings (poured from large bottles into small nursing bottles), Staph. albus, B. bulgaricus and large air cocci; the powdered whole lactic acid milk, Strep. lacticus, large gram-positive bacilli of the B. bulgaricus type and diphtheroids; powdered dextrimaltose, Strep. lacticus. No virulent bacteria were detected in any of the prepared feedings examined. However, cultures made of the feedings while the infants were nursing frequently contained Streptococcus, Staphylococcus, B. mucosus and other pathogens.

Nasopharyngeal cultures were taken from every one who might in any way come in direct or indirect contact with the infants; there were several hundred in all. The typical mixed nasopharyngeal flora was obtained from every one except three nursemaids. These three cultures contained large gram-negative encapsulated bacilli that were mucoid on solid medium. Referring back to the records of the first outbreak, cultures taken from the noses and throats of these nursemaids contained a few Bacilli mucosi, together with other respiratory organisms. Cultures from the nursemaids' throat were again taken, in order to determine whether this encapsulated bacillus had become the established flora or whether it was transitory. Practically pure cultures were again obtained. The bacillus grew luxuriantly both aerobically and anaerobically in all culture mediums. Litmus milk was fermented but not coagulated. The various sugars, dextrose, lactose, salicin, galactose and mannite, were fermented and acidified. Inulin was not fermented. Examination of direct smears from the nasopharynx as well as smears from the cultures revealed a large gram-negative

encapsulated bacillus in pairs and in short chains. The bacillus was nonmotile. This bacillus was morphologically and culturally B. mucosus (Friedländer type).

Cultures made from the stools of these three nursemaids revealed practically pure cultures of B. mucosus. Cultures of the stools of twelve other nursemaids were taken as a control and a large, mucoid colony appeared occasionally on the blood-agar or Endo's plates, but the predominating bacteria were B. coli, B. alkaligenes, Streptococcus, B. coli, large gram-positive and gram-negative cocci and bacilli of the fecal type. Cultures of the stools and vaginal cultures taken from mothers of infants with diarrhea contained a flora similar to that of the control group of twelve nursemaids.

Repeated cultures were taken from the nose, throat and stools of the three nursemaids until it became conclusive that they were carriers of B. mucosus. All were kept off duty, and at weekly intervals cultures were taken again. B. mucosus persisted. The nose and throat department was called in consultation, and tonsillectomy was advised. Two nursemaids had their tonsils removed, and after a few weeks B. mucosus had disappeared from their cultures. The third nursemaid refused tonsillectomy and was given three months' leave of absence and advice with regard to oral hygiene, etc., in order to see whether B. mucosus would disappear under these circumstances. B. mucosus persisted, however, and the nursemaid was not retained in the hospital.

The diarrhea in the infants' nursery completely subsided after the removal of the three nursemaids. However, if they were the cause of the first outbreak, it is difficult to understand why there were not continuous cases of diarrhea during the two months' interval between the two outbreaks, since the nursemaids were on duty during the entire period. However, no case of diarrhea has developed in the nursery for the new-born during the nine months since these carriers of B. mucosus were taken off duty.

BACTERIOLOGIC STUDIES OF THE INFANTS

Intensive bacteriologic studies were made of the infants with diarrhea who were transferred from the maternity nursery to the children's department. These infants were placed in a special ward. Contagious disease procedures were instituted, and an intern, Dr. Irene Newhauser, was placed on continuous duty in this ward. Dr. Newhauser examined the fresh stools macroscopically and microscopically by moist and stained preparations. As in the first outbreak, the stools were surprisingly free from mucus, pus or blood. They were yellow and soft, and only in the severer cases became watery. Only one infant had a mucous bloody diarrhea. Microscopic examination revealed a short,

plump bacillus with rounded ends, surrounded by a capsule. This bacillus was gram-negative and appeared singly, in pairs and in chains. This bacillus appeared in all the specimens, sometimes in practically pure culture and at other times in conjunction with streptococci, B. coli and B. bifidus. Dr. Newhauser examined the material obtained in a number of aspirations from the stomach, nasopharyngeal secretions and mucopurulent material from the throat. All contained the encapsulated bacilli in almost pure culture.

The stools and the material taken from the stomach in a few aspirations were sent to the bacteriologic laboratory for culture. Direct smear examination of the specimens confirmed Dr. Newhauser's observations. No intestinal parasites were found at any time. The specimens were cultured aerobically and anaerobically in veal infusion dextrose broth and on blood-agar plates and aerobically on Endo's medium and in other mediums as indicated. B. mucosus and anhemolytic streptococci were obtained in practically every culture, sometimes one predominating and sometimes the other. B. coli, B. proteus, B. bifidus, M. ovalis, Staph. albus, one type or more in small numbers, were occasionally accompanying organisms. A careful search was again made for strains of the typhoid-paratyphoid groups, the dysentery group, Morgan's bacillus, gas bacilli, etc., but none were found.

The stools of healthy normal infants of the corresponding age were cultured in order to compare the bacterial flora with that of the infants with diarrhea. When the normal infants were breast fed, the stools contained B. bifidus and M. ovalis; when the normal infants were artificially fed, B. coli predominated, although there were many other intestinal organisms.

Nasopharyngeal cultures were taken from the infants with diarrhea and from a control group of normal infants. In both groups a simpler flora was observed than in similar cultures from adults, as might be expected. Staph. albus and Strep. anhemolyticus predominated in both groups of infants. These organisms were accompanied by an occasional pneumococcus, M. catarrhalis, streptobacilli, B. mucosus, diphtheroids, etc. No pure cultures were obtained; nor was it possible to detect any difference between the flora of the ill and that of the healthy infants. There were apparently very few concurrent infections in the infants with acute diarrhea. In one infant otitis media developed; cultures revealed B. mucosus and Streptococcus. In another infant otitis media developed, from which a streptococcus and B. mucosus were recovered, and multiple abscesses on the scalp, from which Staph. albus, B. mucosus and Streptococcus were obtained in cultures.

Cultures of the blood were taken in only a few instances because of the extreme prostration of the infants. Only one was positive, revealing Strep. ignavus in pure culture.

BACTERIOLOGIC OBSERVATIONS AT NECROPSIES

Necropsies were performed on seven of the infants. Cultures were made of the heart's blood, pleural and peritoneal fluid when it was present, intestinal contents, intestinal mucosa, mesenteric lymph nodes, spleen, lung, and any other material indicated by the autopsy. Direct smears of the pathogenic material were examined, and aerobic and anaerobic cultures were made in enriched broth, blood agar and Endo's medium.

Direct smear examination of the intestinal content in every case revealed plump, gram-negative, encapsulated bacilli, varying from the coccoid form to long rods. Chains of gram-positive cocci appeared in five cases. Other bacteria, which were morphologically B. coli, B. bifidus, Staphylococcus, etc., were occasionally found. Smears of the ground tissue (intestinal mucosa, glands, lungs, etc.) revealed the gram-negative encapsulated bacillus and chains of gram-positive cocci, sometimes one predominating, sometimes the other.

Cultures substantiated the observations made on the smears. Culture of the heart's blood revealed the following organisms: Streptococcus in one culture; B. mucosus in one; B. mucosus and Streptococcus in four, in which B. mucosus predominated in three and Streptococcus in one. The culture of the blood from the seventh infant contained B. subtilis, B. coli and Staphylococcus. These organisms were considered contaminates. The streptococci were different strains, typing as Strep. equinus, Strep. nonhemolyticus II and Strep. fecalis according to Holman's classification.

Cultures of the various fluids and tissues revealed the same organisms, that is, B. mucosus and streptococcus predominating and a few B. coli, staphylococci and other bacteria.

Although both B. mucosus and the streptococcus were obtained from the necropsies, direct smear examination, particularly, revealed striking differences in bacteriology. For example, in two infants who came to autopsy on the same morning, the gross pathology was similar, each having early pneumonia, fluid in the chest, enteritis, etc. Smears from one infant, in all the fluids and tissues examined, revealed large numbers of plump, gram-negative, encapsulated bacilli with only an occasional chain of cocci, while the smears from the other infant contained numerous chains of gram-positive cocci with only a few gram-negative bacilli. The difference in the cultures was less striking because the bacillus tended to overgrow the streptococcus.

From the necropsy material it was impossible to determine definitely whether the streptococcus or B. mucosus or the two organisms in conjunction were the etiologic factor in the epidemic. It seems significant,

however, that the lungs in three autopsies in succession contained B. mucosus of the Friedländer type. On the other hand, on gross examination the lungs were not characteristic of Friedländer's pneumonia. This might be explained by the fact that the pneumonia was in an early stage. B. mucosus is rarely obtained from the heart's blood taken at autopsies on children. Therefore, it seems significant that B. mucosus was obtained in five of these six autopsies, once in pure culture. Strains of both organisms were used in virulence tests.

The intestinal mucosa was less involved pathologically than the clinical course of the infection led one to expect. The following description of the intestinal pathology was given by Dr. Otto Saphir.

NECROPSY RECORD

The following gross changes were found in the intestinal lesions: The mucosa of the ileum was red and swollen and in some places finely granular. This membrane was covered with an extensive amount of reddish-gray mucus. Peyer's patches and the lymph follicles were enlarged. Some of the intestines showed several shallow ulcers, which were found to be independent of Peyer's patches and lymph follicles. The margins of the ulcers were only slightly elevated and not undermined. The walls of the ulcers were smooth. The corresponding portions of the peritoneum showed no evidence of nodules. There was no pseudomembrane on the mucosa, nor was any diffuse or localized inflammation or suppuration present. The lesions were found almost entirely in the ileum, and only a very few cases revealed slight involvement of the colon.

Throughout the mucosa and submucosa, many polymorphonuclear leukocytes were found, in addition to lymphocytes and endothelial cells. The lymph follicles and Peyer's patches had somewhat enlarged germinal centers, but no evidence of necrosis or hemorrhage was noticeable within the follicle. In most cases, the inflammatory cells extended into the submucosa, and in only a few instances were polymorphonuclear leukocytes encountered in the media. There was no evidence of tuberculosis in the sections, nor were there any demonstrable lesions characteristic of typhoid. Neither the localization of the lesion nor the gross or histologic observations were suggestive of any form of dysentery.

VIRULENCE TESTS

The virulence of a number of strains of B. mucosus and of Streptococcus obtained from various sources during the outbreak of diarrhea was tested in rabbits by three methods: intravenous injection of broth

cultures; feeding of oats treated with broth cultures, and feeding of broth cultures through a stomach tube. Six rabbits were given intravenous injections with six strains as follows: three strains of B. mucosus from cultures of heart's blood taken at autopsy; one strain of B. mucosus from a nasopharyngeal culture; one strain of B. mucosus from a healthy infant's stool, and a heart's blood culture containing both B. mucosus and an anhemolytic streptococcus. With the exception of the one receiving the nasopharyngeal strain, all the rabbits died within twenty-four hours. Cultures made from the rabbits contained B. mucosus in conjunction with other organisms, particularly with B. coli.

A group of eight rabbits was fed oats treated with a small amount of broth cultures (one strain per rabbit) of the same strains used for intravenous injection, and in addition two broth cultures of streptococci, one from lung tissue obtained at autopsy and the other from the intestinal mucosa. The only rabbit in which diarrhea developed within twenty-four hours was the one that received the combined culture of streptococcus and B. mucosus. Although the seven healthy rabbits were fed the same cultures by stomach tube, none developed diarrhea.

A group of twelve rabbits were fed oats treated with broth cultures of strains of B. mucosus, i.e., two, strains isolated from stools of infants acutely ill with diarrhea, with the result that diarrhea developed in both; four, strains isolated from carriers with the subsequent development of diarrhea in all and death in two; one, a strain from a stool of a normal infant, followed by the development of no ill effect; one, a strain from a plate exposed in the nursery with the development of ill effect; four, strains from various autopsy cultures with the result that two developed diarrhea, one of them dying.

A group of five rabbits was fed oats treated with the following streptococci: two, strains from blood cultures taken at autopsy, and in both diarrhea developed, one dying and the other recovering; three, strains isolated from diarrheal stools, and none of the rabbits had diarrhea.

A third group of seven rabbits was fed with combined B. mucosus and Streptococcus cultures; the two organisms appearing in the original broth cultures of the pathogenic material were not separated. Two were given cultures from autopsy material, which caused diarrhea, one rabbit dying; four were given cultures from acutely ill infants and diarrhea developed in three, one dying; one was given a culture from a carrier, and diarrhea and death resulted.

Minute doses of broth cultures of B. mucosus or of Streptococcus injected intraperitoneally into mice proved fatal within twenty-four hours.

The virulence experiments with rabbits indicated that the strains of B. mucosus and of Streptococcus isolated in this epidemic of diarrhea,

alone and in combination, could produce diarrhea or death in rabbits. The two organisms combined were the most virulent, and next in order was B. mucosus; the anhemolytic streptococcus was the least pathogenic.

The infants with epidemic diarrhea appeared even more toxic than the degree of diarrhea warranted. Therefore the toxicity of the strains was studied by Shwartzman's phenomenon of local skin reactivity. A Berkefeld filtrate of the bacterial strain in question is made, and 0.25 cc. is injected intracutaneously into the skin of the shaved abdomen of a rabbit; from twenty to twenty-four hours later, 2 cc. is injected intravenouly into the same rabbit; if the filtrate is toxic, a hemorrhagic area appears within five hours at the site of the skin injection. Filtrates of seven strains of B. mucosus and of five strains of streptococci were prepared and used as described. A filtrate of a strain of B. mucosus isolated from a carrier gave a weakly positive reaction. All the other tests were negative. Therefore, according to the Shwartzman test for toxicity, these strains of B. mucosus and of Streptococcus did not produce toxin.

AGGLUTININ TESTS

A small amount of blood was withdrawn from one of the infants who had recovered from the infectious diarrhea. This serum agglutinated six B. mucosus strains as follows: an autopsy strain and a carrier strain in a 1:40 dilution of serum, a strain obtained from the exposed agar plate in the nursery in a 1:80 dilution of serum and a strain isolated from a rabbit at autopsy in a dilution of 1:10. The infant's serum was tested with five strains of streptococci. One autopsy strain was agglutinated in a 1:80 dilution of serum. The other tests were negative.

One infant who had apparently recovered from diarrhea returned after two months with a mild diarrhea. B. mucosus was again isolated from the stool. A sample of blood was obtained from the infant, and agglutination tests made with the strain of B. mucosus isolated from its stool and with several other strains of B. mucosus. These were agglutinated in a 1:40 dilution of serum. The other organisms (streptococci, etc.) were not agglutinated. The agglutination tests indicate that agglutinin was elicited for B. mucosus and to a slight degree for streptococcus in the serum of the infants recovering from diarrhea.

RESULTS OF BACTERIOLOGIC STUDIES

This outbreak of diarrhea was not due to any of the organisms commonly associated with diarrhea. Typhoid bacilli, paratyphoid bacilli, dysentery bacilli, gas bacilli, Bargen's diplococci, enterococci and Morgan's bacilli were definitely ruled out as the etiologic factor of the disease. B. mucosus and various anhemolytic streptococci were isolated

from antemortem and postmortem material from the infants. Streptococcus and B. mucosus either in conjunction or separately have been known to cause enteritis. It is possible that this outbreak was a concomitant infection, since both organisms were so uniformly found in all cultures, and since the two organisms in combination were more pathogenic to rabbits than either separately. The universality and pathogenicity of an anhemolytic streptococcus render it impossible to rule out this organism as an etiologic factor of the epidemic, even though a number of strains were isolated. Although B. mucosus is ordinarily a saprophyte in the intestine, it is well known that it may take on pathogenicity and cause enteritis (Zinsser [2] and Kendall [3]). The tests for virulence indicated that the strains of streptococci were virulent for rabbits and that all the strains of B. mucosus isolated and tested from nasopharyngeal cultures, from the nurseries and from the antemortem and postmortem specimens from the infants were pathogenic for rabbits. A combination of the two organisms apparently increased this virulence. The fact that B. mucosus was found in cultures of heart's blood and lung tissue, an uncommon site for this organism, points to this organism as the cause of the infection.

Agglutination reactions with the serum from two convalescent infants did not indicate conclusively which organism was the causative factor, since a number of the strains of B. mucosus and one strain of streptococcus were agglutinated.

The most positive evidence for suspecting that B. mucosus was the etiologic organism was the fact that it was found in practically pure culture in the nasopharyngeal cultures from three nursemaids, and that after the removal of these carriers from the nursery no new cases of diarrhea developed over a period of nine months. On the other hand, it is difficult to explain why there was a two month's remission in the diarrheal outbreak, if these carriers were responsible for the infection, since they were on duty during the entire period. However, examination of their nasopharyngeal cultures in the early period showed B. mucosus as one of a variety of organisms present, while in the severe outbreak (April and May) the bacillus appeared repeatedly in almost pure culture. It is possible that the organisms increased in virulence as well as in number.

At present, it seems probable that this outbreak of diarrhea in the new-born was caused by B. mucosus, and that its severity was augmented by the presence of streptococci.

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2. Zinsser, Hans: A Textbook of Bacteriology, New York, D. Appleton and Company, 1928, p. 614.

3. Kendall, Arthur I., and Day, Alexander: Observations on Summer Diarrheas in Children, Boston M. & S. J. **169**:753, 1913.

III. SUMMARY

By Drs. Jampolis, Howell, Calvin and Leventhal

1. An outbreak of infectious diarrhea developed in a nursery for the new-born. This outbreak spread insidiously. A latent period of two months elapsed after the first few cases appeared.

2. The constitutional symptoms, severe intoxication, dehydration and prostration, were out of proportion to the relatively mild diarrheal symptoms.

3. The stools averaged about six daily. They were watery and contained mucus but no blood or pus, except in one case.

4. The mortality was high in spite of the usual accepted treatment for anhydremic intoxication.

5. Apparently the offending organism was B. mucosus, the virulence of which may have been enhanced by symbiosis with anhemolytic streptococci. B. mucosus was isolated from the nasal secretions, stomach contents, stools and intestinal mucosa in a large number of the cases. None of the usual organisms causing infectious diarrhea, such as the typhoid-dysentery groups, was found.

6. The primary and outstanding pathologic findings in the fatal cases consisted of acute enteritis, the mucous membrane of the ileum being red, swollen, finely granular and covered with reddish-gray mucus. Microscopic examination showed the mucosa to be infiltrated with polymorphonuclear leukocytes and lymphocytes. A few shallow ulcers were found, and the lymphoid tissue was hypertrophied. However, there was a relative absence of involvement of the colon, which probably accounts for the comparatively few diarrheal stools and the absence of pus and blood.

7. In only a few instances was there evidence of parenteral infection. In a few babies terminal bronchopneumonia and otitis media developed. Cultures from discharge of the ears and the lungs in these cases revealed the same organisms as were found in the intestinal lesions, namely, B. mucosus and anhemolytic streptococci.

8. Repeated cultures from the throat and stool of three nursery maids revealed practically pure cultures of B. mucosus. When these nursery maids were relieved of their duties in the nursery, the outbreak promptly subsided, and there has been no recurrence during the past nine months. Cultures from two of these girls became negative a few weeks after tonsillectomy. The third one refused operation, and the cultures remained positive.

9. For the past few years pediatric literature has contained numerous accounts of outbreaks of diarrhea similar to the one described here. They

are usually attributed to parenteral infections, for the most part, respiratory diseases and otitis media. The parenteral infection is usually held responsible for the severe general symptoms, and the diarrhea is considered secondary and incidental. The investigations reported in this article apparently point out that diarrhea accompanied by marked prostration, dehydration and intoxication may be due to primary enteritis even though the stools do not show pus or blood.

10. The outstanding features reported are: (*a*) B. mucosus, as the etiologic agent in severe infectious diarrhea, (*b*) nursery-maids as carriers, (*c*) the relative absence of parenteral infections, and (*d*) the absence of the bloody, purulent stools that are considered characteristic of infectious diarrhea.

A NEW METHOD OF RECORDING CHILDREN'S FOOTPRINTS *

HELEN KING
DETROIT

Impressions of the foot have usually been taken in a standing position, but such an imprint may not always be the natural one. A consciousness in placing the feet in a definite standing position may lead to an unnatural distribution of weight as well as an artificial position of the feet. The procedure described in this paper for obtaining and recording natural standing and walking footprints has contributed significant information on the correlation of the physical growth and development of children. Although it is now recognized that impressions of the foot are not of any great value for diagnostic purposes, they are of definite value in showing changes in the musculature of the feet and the efficiency of proper footwear and hygiene of the feet for children.

Lewin [1] expressed the belief that the value of footprints has been overestimated from the standpoint of both diagnosis and prognosis. He pointed out that the footprint of the new-born infant is inadequate and misleading, in that it usually looks flat because the bony arch is obliterated by a pad of fat. In fact, the foot of the new-born infant reveals, in cross-section, a definite bony arch, but in a position of pronation to which the term pes cavus valgus may be applied. Not until the child is about 3 years old does the footprint show much of significance about the actual condition of the foot. But after this age, the prints are of value in studying changes in the musculature of the feet.

The recording of children's footprints, especially as a part of the physical growth and development records of the child development centers, presents some difficulties. The customary single standing print, for instance, may be unsatisfactory, owing to a consciousness in placing the feet which may lead to an unnatural distribution of weight, as well as an artificial position of the feet. Further, even supposing the foot to be in its natural weight-bearing position, it is difficult to secure an accurate and detailed print. After studying the foot by the plate glass and mirror method, showing both the weight-bearing and line of contact surfaces, Lovett and Jones [2] concluded that both the smoked

* Submitted for publication, April 14, 1931.
* From the Merrill-Palmer School.

1. Lewin, Philip: Orthopedic Surgery for Nurses, Philadelphia, W. B. Saunders Company, 1928.

2. Jones, Robert, and Lovett, Robert W.: Orthopedic Surgery, New York, William Wood and Company, 1923, p. 603.

tracing and the wet tracing of the foot are unreliable for purposes of study, because they record the nonweight-bearing position before the weight-bearing position, and so show a composite of the two.

In studying and recording the condition of the feet of the children of the Merrill-Palmer nursery school, as a part of their physical growth and development records,[3] it became evident that the walking footprint offered the best means of obtaining a record of the natural standing position of the feet, as well as an accurate record of the position of the feet in walking. A satisfactory procedure for making the prints has been worked out after some experimentation.

PROCEDURE

Several factors must be considered in recording footprints: The method must be quick and simple and must insure a record of the natural position of the feet in walking and in standing, and the impression should be detailed and permanent. Even the printing process

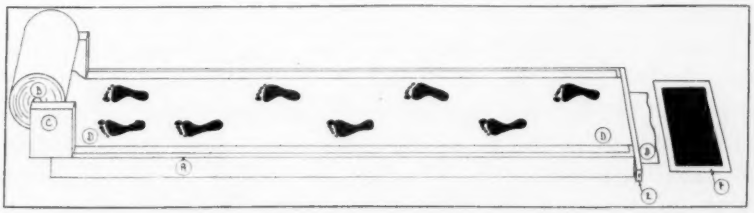

Fig. 1.—The board walk on which footprints are recorded. *A*, wooden frame; *B*, roll of paper; *C*, paper holder; *D*, strip of paper from roll; *E*, paper holder and cutter; *F*, bristol board to which Flak Finger Print Ink has been applied.

offers difficulties.[4] The substance used must be sufficiently adherent to last while the child takes half a dozen steps and at the same time print well enough to show a detailed impression of the foot at each step.

Several methods of recording foot conditions were tested before the present procedure was adopted. At first plaster casts of the children's feet were made, but this method was abandoned when it was found that the weight-bearing position could not be recorded in this way. X-ray photographs of the feet, in both weight-bearing and nonweight-bearing

3. Sweeny, Mary E.; King, Helen; Wilson, Charles A., and Hejinian, Lucea: A Method of Recording the Posture of Preschool Children, Detroit, The Merrill-Palmer School, 1929.

4. Brahdy used Freiberg's solution of ferric chloride, alcohol and glycerin, applying the solution to the soles of the feet and taking the weight-bearing imprints on rough paper. The prints were then darkened and preserved with a solution of tannic acid. (Brahdy, M. Bernard: Flatfoot in Children, Arch. Pediat. **44**:86 (Feb.) 1927.).

positions, were made for a time. These photographs probably give more information about the relations of the bones in the weight-bearing and nonweight-bearing positions than does any other record; but unless the elaborate equipment necessary for taking the photographs is used for other purposes as well, the expense of this kind of record makes it impracticable except for the study of unusual cases. The method of recording both the weight-bearing and the nonweight-bearing positions of the feet on white Bristol board, with such solutions as lampblack

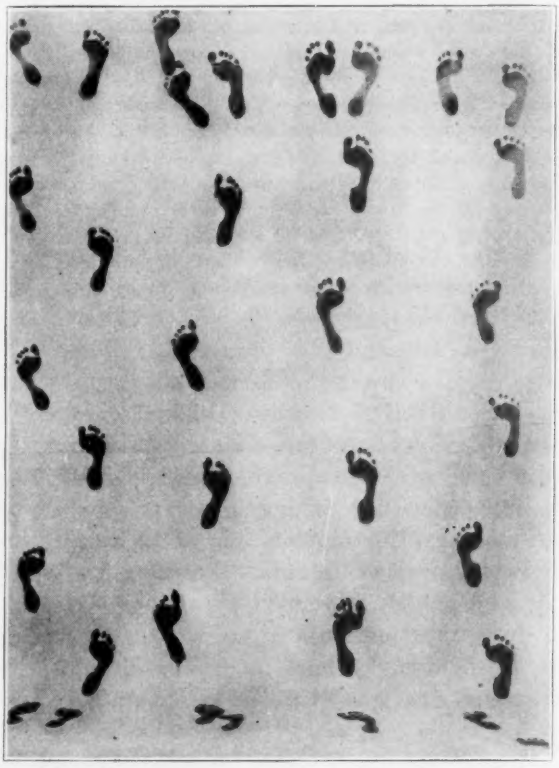

Fig. 2.—A record of walking and standing footprints.

with a fixative, black finger print powder or a tincture of iron chloride in alcohol and glycerin (55 cc. of tincture of iron chloride, 45 cc. of medicated alcohol and 10 cc. of glycerin) was tested. Of these solutions the last proved the most satisfactory, though it was not entirely so.

The apparatus and method finally adopted may be briefly described.

The apparatus (fig. 1) consists of a "board walk" 6½ feet (198 cm.) long, framed with sides measuring 1½ inches (3.77 cm.), and covered with beaverboard.

At one end is built a support for a roll of white wrapping paper 12 inches (30.48 cm.) wide, placed on the usual revolving rod. The paper is drawn down the length of the board, threaded through a slit in the frame, and held in place by a wooden bar that is hinged at one end so that it can be raised or lowered as the paper is drawn through. The paper is torn off against a tin strip on the bottom of this bar.

Flak Finger Print Ink,[5] which comes in tubes and has the consistency of oil paint, was found most satisfactory of the various printing materials tested. The ink dries quickly, does not smudge and makes a detailed and permanent print.

The procedure of taking the print is as follows: On the floor near the foot of the board walk is placed a small square of bristol board on which a little of the finger print ink is squeezed and rolled out smoothly and thinly with a short rubber roller. The child stands on this inked paper and then steps on the paper on the board walk and walks to the head of the board, where he stands with his feet parallel to each other and is lifted off. Thus both a standing impression and a walking impression of the feet are recorded. The paper is then drawn down the length of the board and torn off, and the board is ready for the next child's footprints. The strip of paper is dated, signed with the child's name or registration number and folded and kept in a file. About three minutes are required to make the record. Several of these record strips are fastened on a wall and photographed together (fig. 2), and the photographs are then cut into individual strips. This small print of the footprint record, measuring 3½ by 4½ inches, is filed with the other records of the child's physical growth and development.

SUMMARY

A satisfactory method of recording children's walking and standing footprints has been developed at the Merrill-Palmer School. The essentials of the method are the use of Flak Finger Print ink and of a board walk equipped with wrapping paper as the printing materials. All details of the sole of the foot and toes in the weight-bearing position are shown. Photographs of the strips measuring 3½ by 4½ inches are kept in a file as a part of the child's physical growth records. Prints recorded in this way at intervals of six months show the growth and development of the foot, changes in gait position and the results of corrective exercises in cases of weak musculature and pronation.

5. Obtainable from Flak Finger Print Ink Company, Inc., Liberty Street, New York City.

PAROXYSMAL TACHYCARDIA IN CHILDREN

REPORT OF FOUR CASES AND ONE POSTMORTEM EXAMINATION *

CHARLES SHOOKHOFF, M.D.

ABRAHAM M. LITVAK, M.D.

AND

IRVING MATUSOFF, M.D.

BROOKLYN

The occurrence of paroxysmal tachycardia in infancy and childhood has been considered extremely rare. In recent years the number of such case reports has been definitely increasing. Willius and Amberg,[1] in 1929, gathered twenty-five cases from the literature including a case of their own. In 1930, Essig [2] added ten cases to that number. Van Cleve [3] recently reported a case in an infant. The four reports in this paper bring the number of instances of paroxysmal tachycardia in children in the literature up to forty. This increasing number of case reports is due probably to the more general use of the electrocardiogram in the clinic and to the greater interest in cardiovascular diseases. We feel that paroxysmal tachycardia in children is more common than the dearth of the literature would lead us to believe. Many instances of this disorder have undoubtedly been overlooked because of the mildness of the symptoms and because of symptoms referable to other organs than the heart. Adults suffering from paroxysmal tachycardia not infrequently give a history of having had attacks since childhood (Edens [4]). A woman (treated by one of us), aged 67 years, the mother of a physician, gave a history of having had attacks since the age of 10 years. No age period, it seems, is exempt. The youngest patient whose case has been reported was a child 4 days old (Werley [5]).

The four cases reported here are of interest because they were observed in a relatively short time. Cases 1, 2 and 4, we believe, are

* Submitted for publication, March 26, 1931.

* From the Cardiological and Pediatric Departments of the Jewish Hospital of Brooklyn.

1. Willius, F. A., and Amberg, S.: Paroxysmal Tachycardia with Syncope Occurring in a Child, Am. J. Dis. Child. **37**:551 (Sept.) 1929.

2. Essig, B.: Paroxysmale Tachykardie im Kindesalter, Monatschr. f. Kinderh. **48**:288, 1930.

3. Van Cleve, M.: A Case of Paroxysmal Tachycardia in an Infant Seven Months Old, J. A. M. A. **96**:1758 (May 31) 1930.

4. Edens, E.: Die Krankheiten des Herzens und der Gefässe, Berlin, J. Springer, 1929, p. 485.

5. Werley, G.: Paroxysmal Tachycardia with a Ventricular Rate of 307 in a Child Four Days Old, Arch. Pediat. **62**:825, 1925.

instances of paroxysmal auricular flutter, and case 3, a case of simple paroxysmal auricular tachycardia. Case 4 is of interest because the first attack lasted about twenty-four days and ended fatally. Necropsy findings are reported. Although we were not able to register the beginning and the end of the attacks, it is felt these cases throw some light on the differential diagnosis between paroxysmal tachycardia and paroxysmal auricular flutter with 1 : 1 rhythm. The latter is the more common type in children. This differentiation, however, is only of academic interest, since all types of paroxysmal tachycardia in children seem to be associated with myocardial disease. The attacks in case 3 are attacks of paroxysmal auricular tachycardia, and were apparently the earliest manifestations of a severe active rheumatic fever. In at least three of the cases the impression that myocardial disease is an underlying cause seems justifiable.

REPORT OF CASES

CASE 1.—*History.*—A. K., aged 8 years and 6 months, was brought to the Children's Cardiac Clinic of the Brooklyn Jewish Hospital on Nov. 11, 1930. The chief complaints were abdominal cramps and vomiting. The child was delivered at full term; the birth weight, feeding and developmental history were normal. The patient had mumps at 3 years of age, and influenza at 6 years of age, following which a dry croupy cough persisted for many months. There were no other illnesses. The mother, 40 years of age, was alive and well; she had four normal pregnancies and her children were normal. The father, aged 42 years, was alive and well. The maternal grandmother died of "heart disease."

In May, 1930, the patient was awakened by a generalized pain throughout his abdomen and a feeling of nausea and dryness in the mouth. He vomited on taking water. After this he vomited frequently for about six hours. The mother called a physician who noticed that his heart was "running fast." After forty-eight hours all the patient's symptoms disappeared, and the cardiac rate was normal. Following this attack, the patient was apparently well. He was a physically active child, did not tire or complain of shortness of breath and slept well. The bowel movements were regular. On November 10, the day before his first admission to the clinic, the patient again suddenly complained of abdominal cramps, vomiting and palpitation.

Physical Examination.—On admission to the outpatient cardiac clinic, examination showed a fairly well built child weighing 55¼ pounds (25,060 Gm.) and measuring 47¾ inches (121.3 cm.) in height. The temperature was 100.2 F. rectal. There was left internal strabismus. The nasal septum deviated to the right. The teeth were decayed, and the roots badly infected. The tonsils were hypertrophied, cryptic and infected. The submaxillary glands were enlarged, especially the right. The cervical veins were distended and pulsating. The chest was fairly well formed, with a slight flair of the lower ribs. There was a short blowing systolic murmur at the apex of the heart, which was transmitted to the left axilla; the second pulmonic sound was not accentuated. The point of maximum intensity was 5.5 cm. from the midsternal line in the fifth interspace; the left border in the fourth interspace was 6 cm. from the midsternal line, and the right border in the fourth interspace 2.5 cm. from the midsternal line. The cardiac rate was very high and not influenced by change of position, deep breathing, carotid sheath, oculobulbar pressure or exercise. The vesicular note was

normal throughout the lungs; there were no râles. No tenderness or masses were felt in the abdomen; the liver and spleen were not palpable. The extremities were normal; there was no edema. The knee-jerks were hyperactive. The parent refused hospital care, and the patient was taken home.

Electrocardiogram.—Figure 1 shows an auricular ventricular tachycardia with a 1:1 conduction and a rate of 225. The T and P waves cannot be differentiated; the ventricular complexes are normal. In lead I, by continuing the downward stroke of the positive auricular wave between two ventricular complexes, one can see definite regular movements of the iso-electric line at the rate of 225 per minute (fig. 2). This constant rhythmic movement of the iso-electric line is, we believe, evidence of flutter. The difference in the spacing between the auricular waves is almost negligible.

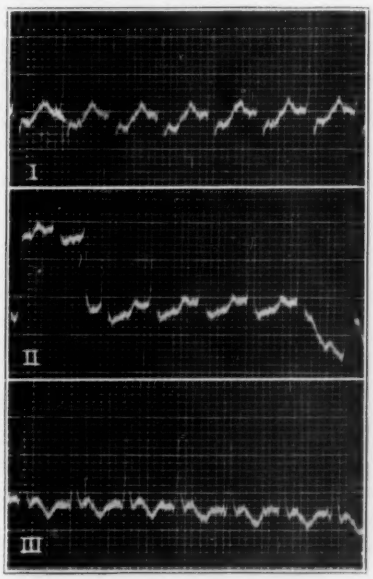

Fig. 1 (case 1).—Electrocardiogram of patient A. K.; rate 225, in attack.

Subsequent Course.—On November 30, the patient again visited the cardiac clinic. The attack of November 10 had lasted until the evening of the eleventh. Since that time the patient had been well. Physical examination revealed no abnormalities.

Electrocardiogram.—Figure 3, taken on the second visit, shows a regular sinus rhythm with a ventricular rate of 103. The P waves of lead II are rather prominent; the T waves of lead II are of low voltage. T_3 is inverted. The P-R interval is 0.14 second.

The patient was advised to return for the removal of infected tonsils and teeth.

Subsequently, this patient was reported to have had another short attack which ended spontaneously.

Comment.—This boy was well up to the age of 6 years when an infection of the upper respiratory tract developed that was of longer

than normal duration, and as a sequel a cough developed which lasted for many months. There were no other illnesses. The boy had badly infected and decayed teeth and large cryptic, hypertrophied tonsils. His first attack occurred a short time after the end of a pulmonary bronchial infection. The symptoms in this attack were nausea, vomiting, abdominal cramps and rapid heart action. The electrocardiograms made during the

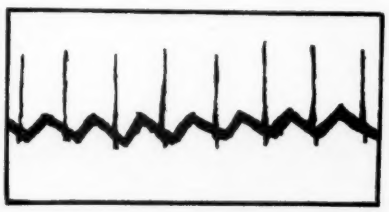

Fig. 2 (case 1).—Diagrammatic reconstruction of lead I (fig. 1) showing the regular continuous movement of the base line, not obscured by the ventricular complexes.

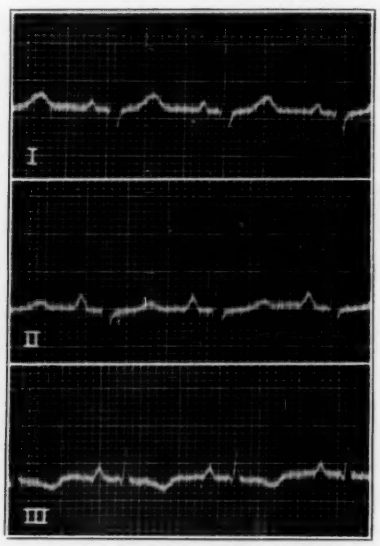

Fig. 3 (case 1).—Electrocardiogram of patient A. K.; regular sinus rhythm.

attack show an auricular flutter with a flutter rate of 225 and full conduction. No medication was given. The attacks stopped spontaneously, the longest lasting forty-eight hours. There was no evidence of cardiovascular disease between attacks. The electrocardiogram taken on November 30, nineteen days after his last attack, shows a rather prominent P wave and a low voltage T in the second lead with an inverted T in the third lead. This finding is not usually seen in normal

children of this boy's age (Shookhoff and Taran [6]), and might be considered evidence of some myocardial disturbance. The prolonged bronchopulmonary disease might have been a causal factor.

No laboratory data other than the electrocardiographic studies were available.

CASE 2.—*History.*—S. S., a girl aged 3 years, was admitted to the Jewish Hospital on Feb. 24, 1930, and was discharged on March 6.

She was delivered at full term. The birth weight, feeding and developmental history were normal. She had varicella at 1 year and pertussis at 2 years of age. She coughed and whooped for about six weeks. Her paroxysms, however, were not unusually severe. One year before admission to the hospital, while still convalescing from pertussis, she was suddenly seized with weakness, cardiac palpitation and epigastric discomfort. She vomited repeatedly, and the mother noticed rapid pulsations of the veins of the neck. This attack lasted four days and disappeared as suddenly as it came. Since then attacks of rapid heart action, epigastric distress and vomiting have recurred at intervals of from two weeks to two months and have varied in duration from a few hours to days. The onset and termination of these attacks were not determined by any known factor. In the intervals between attacks, the child was apparently well.

On February 20, four days before admission to the hospital, the present attack began suddenly. The child felt weak, became dyspneic on exertion, complained of epigastric pain and vomited several times, and the mother noticed that the child's heart beat fast. Although the gastric symptoms had abated after the first two days, the rapid heart rate still continued, and the child was admitted to the hospital on Feb. 24, 1930.

Physical Examination.—On admission the child appeared to be well nourished and well developed; she was lying on her back and was dyspneic and listless. Her cheeks were slightly flushed. The head, eyes, ears and nose were normal. The veins of the neck were full and pulsating. The pharynx was somewhat congested and the tonsils were moderately enlarged and cryptic. The lungs were normal. The heart was slightly enlarged to the left and right on percussion. There were no thrills. The rate was regular, but so rapid that it could not be counted. No murmurs were heard. The respirations were rapid, between 30 and 40 per minute. The radial pulse was almost imperceptible. Some tenderness and spasticity were present in the right upper quadrant of the abdomen. The liver edge was two and a half fingerbreadths below the costal margin, and was tender; the spleen was not palpable. The extremities were normal. No blood pressure readings could be obtained.

Clinical Data.—The urine was normal. There were 14,300 white blood cells with 83 per cent polymorphonuclears. Cultures of the nose and throat were negative for Klebs-Löffler organisms. The Wassermann and Kahn tests were negative. The sugar tolerance test during fasting showed 123 mg. of blood sugar per hundred cubic centimeters. Thirty-eight grams of dextrose in 100 cc. of orange juice was given; after one-half hour the blood sugar was 174 mg.; after one hour, 185 mg.; after two hours, 190 mg.; after three hours, 173 mg. The delay of the curve to return to normal might be explained by the diminished functional activity of the liver to form or store glycogen due to the congestive changes in this organ, as evidenced by the enlargement and tenderness.

6. Shookhoff, C., and Taran, L. M.: Electrocardiographic Studies in Infectious Diseases: I. Normal Children, Am. J. Dis. Child. **42**:342 (Aug.) 1931.

Roentgen Examination.—On admission the heart showed a slight degree of broadening of the upper left cardiac outline. There was no other abnormality. The lungs showed no pathologic process (fig. 4).

Electrocardiogram.—Figure 5, taken on admission, shows an auricular ventricular tachycardia with a rate of 270. A definite alternation is seen in the second and third leads. In the first and third leads the regular rhythmic movements of the iso-electric line are seen. Figure 6 is a diagrammatic scheme of lead I of figure 5 showing the reconstructed base line. The difference in the time spacing between the auricular waves is almost negligible. The T and P waves can not be differentiated. An electrocardiogram taken two and three days later showed the same ventricular and auricular rate, 270 per minute. There was present, however, a right axis deviation.

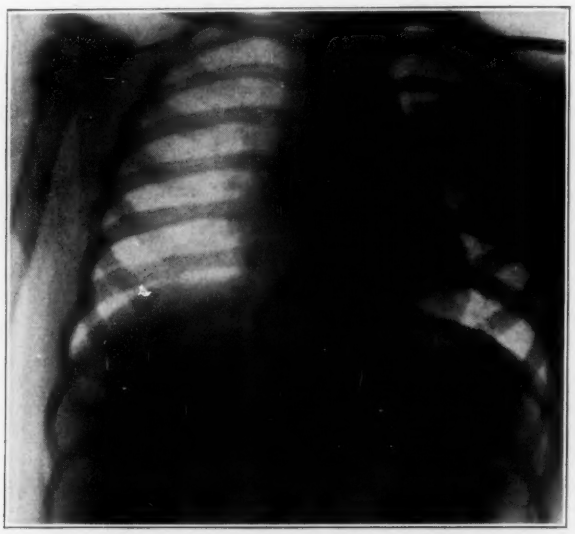

Fig. 4 (case 2).—Roentgenogram taken on the sixth day of the attack.

Oculobulbar pressure, carotid sheath pressure, right and left, induction of vomiting, and all the other sinus reactions were used without effect. On this day another electrocardiogram (fig. 7) was taken after the administration of quinine bisulphate, 4 grains (0.26 Gm.) intravenously. This shows a slowing of the ventricular rate to 200 per minute and a widening of the Q-R-S group. The tachycardia had not stopped. The patient was then given 6 cc. of tincture of digitalis at one time and 6 cc. in divided doses within eighteen hours. The following morning, February 28, the heart rate had slowed down to 120, no irregularity being noted, and thereafter to 90 per minute. An electrocardiogram (fig. 8) taken shortly after shows a normal sinus rhythm with a ventricular rate of 105. The T waves in lead I are iso-electric and in lead II, of low voltage; the P waves are rather prominent, and the P-R interval is 0.16 second. There is no abnormal axis deviation. The child ceased to vomit, began to ask for food, and became brighter; the liver decreased in size, and the abdominal tenderness had disappeared.

The temperature varied between 99 and 100 F. the first week of the patient's stay in the hospital. Despite the extraordinary rate at which the heart was

racing for twelve days, the patient was relatively comfortable, showing only slight evidences of cardiac decompensation, enlargement of the liver and faint cyanosis. The early symptoms of nausea and vomiting disappeared after the first two days of the tachycardia.

At the time of discharge, March 6, the heart was normal in size; the sounds were of good quality and there was a third sound at the apex. No murmurs were heard, and the liver had receded to the costal margin.

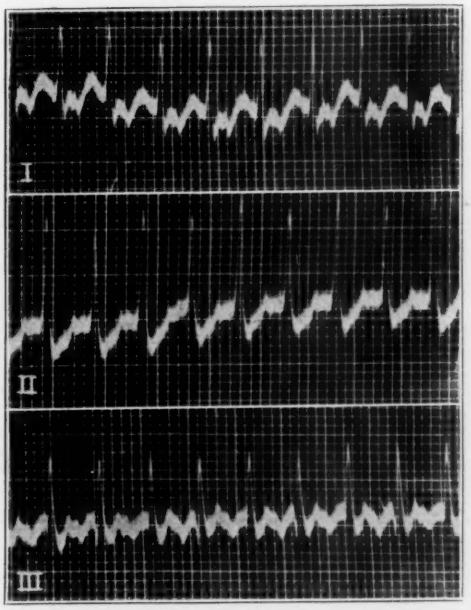

Fig. 5 (case 2).—Electrocardiogram showing an auricular and ventricular rate of 270. Alternation is seen particularly in the second and third leads.

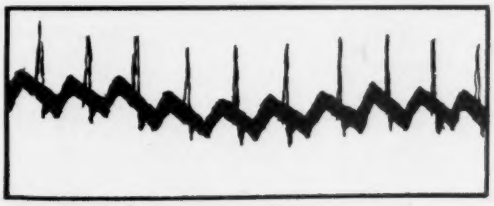

Fig. 6 (case 2).—Diagrammatic reconstruction of lead I (fig. 5) showing the regular continuous movements of the base line, not obscured by the ventricular complexes.

Subsequent Course.—On March 28, while at play, the child was again seized with a similar attack which came on suddenly; vomiting, epigastric pain, rapid heart rate, large and tender liver and listlessness were noted. One-fourth grain (16 mg.) of phenobarbital was given; the child slept well. The next morning the heart rate was normal. The blood pressure was 90 systolic and 60 diastolic;

the heart rate was 110. The liver was still enlarged; the lungs were clear, and the child was quite comfortable.

Examination on April 5, at the Children's Cardiac Clinic of the Jewish Hospital revealed good general condition. The heart rhythm was regular, with a

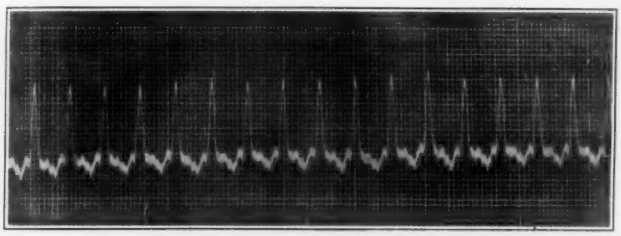

Fig. 7 (case 2).—Electrocardiogram taken after the injection of 4 grains of quinine bisulphate intravenously. The ventricular rate here is 200 per minute. Note the widening of the Q-R-S complex, the slurring of the R and the slowing of the ventricular rate.

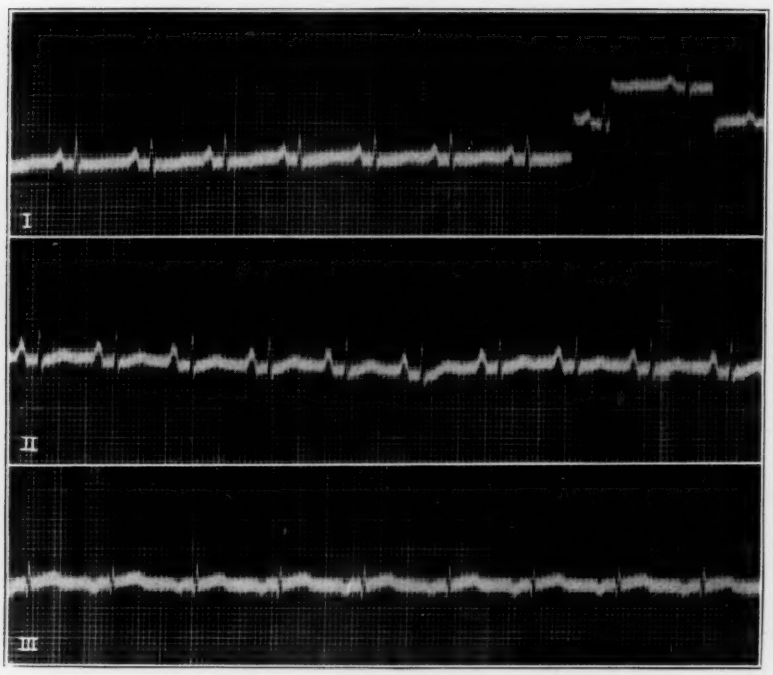

Fig. 8 (case 2).—Electrocardiogram showing normal sinus rhythm the day following the cessation of an attack after digitalization. The T wave changes are most likely due to digitalis.

rate of 90 per minute. No evidence of cardiac enlargement was noted by percussion. At the apex there was a short, medium-loud systolic murmur that was not transmitted; the second pulmonic sound was accentuated. The liver was not enlarged.

After this the patient had frequent attacks with similar symptoms, the attacks lasting from a few hours to several days and coming on as frequently as two or three times a week. Electrocardiograms taken in these attacks always showed similar conformations of the auricular waves and a ventricular and auricular rate of about 270.

Electrocardiogram.—Figure 9, taken on April 18, shows a sinus arrhythmia, with an average ventricular rate of 100. The T waves are all normal, and the relationship between the height of the P and T is normal. There is no abnormal axis deviation. This graph was taken one day after the patient had an attack lasting sixteen hours.

Roentgen Examination.—Figure 10, taken on the same day, shows a more pronounced bulging of the pulmonary curve, suggestive of an increasing interpulmonary pressure.

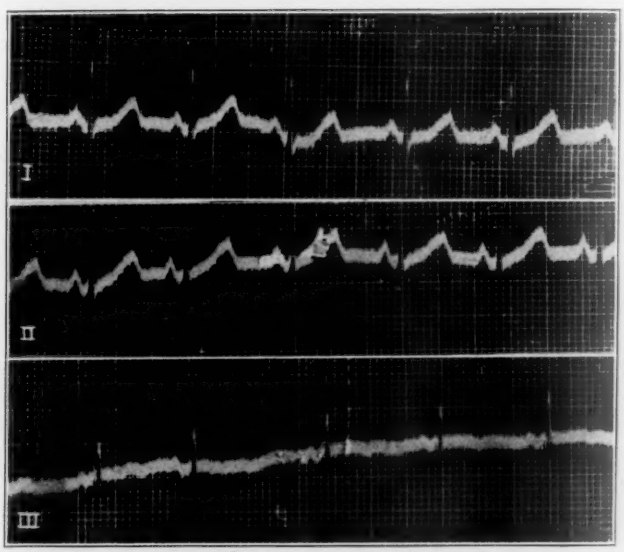

Fig. 9 (case 2).—Electrocardiogram showing normal sinus rhythm, taken after an attack lasting eighteen hours. No digitalis was given. Note the difference in the height of the T wave as compared with that in figure 8.

Physical Examination.—On April 19, there was slight enlargement of the left ventricle. The second pulmonic sound was accentuated and split; the first sound at the apex was loud, and there was a soft blowing systolic murmur at the apex and base that was not transmitted. The rate was 80 per minute. The liver was not enlarged and the child's general condition was fair.

Owing to the frequency of the attacks, it was advised that the large infected tonsils be removed. This was done at the Jewish Hospital on June 9, and the patient went through this operative procedure uneventfully. Since then she has been under constant observation and has been having attacks just as frequently and of the same duration as before the tonsillectomy. The attacks end spontaneously, and no medication, quinine, digitalis, etc., appears to influence the frequency of the attacks or the duration of the individual attacks.

Comment.—This child, while convalescing from pertussis, experienced her first attack of paroxysmal tachycardia. The constancy of auricular and ventricular rate in every attack (about 270), the movements of the iso-electric line as seen in leads I and II showing constant activity in the auricular musculature, alternation of the ventricular complexes, particularly seen in the second and third leads, and the cessation of the second attack after digitalization in various rate stages, all speak for the diagnosis of auricular flutter with a 1 : 1 conduction time rather than a paroxysmal auricular tachycardia. Every possible method of treatment was used without avail. The longest attack lasted over six

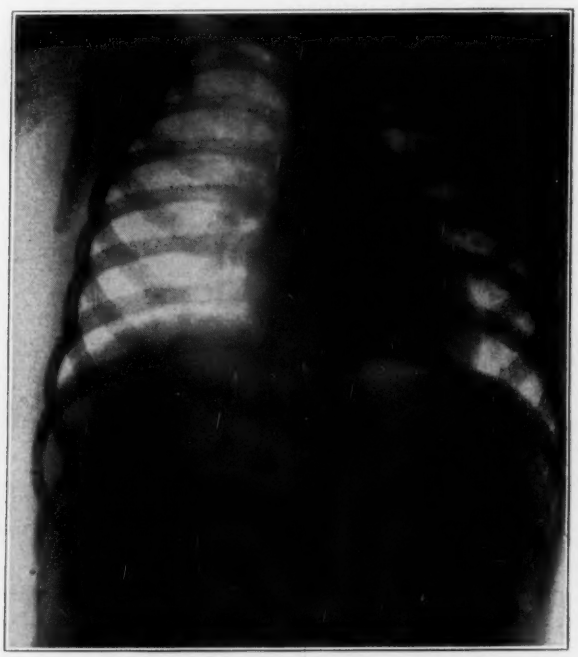

Fig. 10 (case 2).—Roentgenogram taken on April 18, 1929, showing a more prominent bulging of the pulmonary curve, suggestive of increasing intrapulmonary pressure.

days and stopped after complete digitalization. Quinine bi-sulphate, intravenously, caused a slowing of the ectopic rate but did not end the attack.

The frequency of these attacks, the inability to influence the occurrence or length of them by medication, and the gradually increasing evidences of myocardial damage—appearance of murmurs and bulging of the pulmonary curve—seem to indicate a definite progressive myocardial lesion. The flat T_1 and the low voltage T_2 in figure 8 (a curve taken immediately after a long attack and complete digitalization) seem,

however, to be due to digitalization rather than to myocardial fatigue. Figure 9 (curve taken shortly after an attack lasting sixteen hours, no digitalis given) shows normal T waves in all leads.

CASE 3.—*History.*—R. E., aged 10 years and 3 months, was admitted to the hospital on Jan. 23, 1928, and discharged against advice on Feb. 11, 1928. The chief complaints were fainting spells for four weeks, dyspnea, palpitation, tachycardia and nervousness, and fatigue on exertion. The family history was unimportant. The child was delivered normally and development had been normal. She had pertussis at 1 year of age, which lasted three months. She had measles at 2 years and varicella at 2½ years. There was no history of diphtheria, scarlet fever, mumps, rheumatism, muscle or growing joint pains or epistaxis. She had frequent attacks of tonsillitis and sore throat for four years. Tonsillectomy and adenoidectomy were performed at the Jewish Hospital in May, 1927. In 1923, the patient had a third degree burn of the lower half of the body; at this time some mention of a cardiac murmur was made.

Three months before admission to the hospital, following some exertion at school, the patient complained of feeling especially tired. The family physician found her heart beating very fast, and she was put to bed for one month. When she was allowed out she became dyspneic, pale and had a rapid heart rate. In the four weeks before admission she had syncopal attacks with complete loss of consciousness. These attacks occurred suddenly, lasted from five to ten minutes and were followed by dyspnea and a choking sensation. Attacks have occurred as frequently as three and four times a day.

Physical Examination.—On admission, the temperature was normal; the pulse rate, 190, and respirations, 24. The child was very apprehensive. The head, eyes and ears were normal. The face was flushed and slightly cyanotic. The mouth and throat were normal. The posterior cervical glands were palpable. The jugular vessels were pulsating forcefully. The lungs were clear. There was a diffuse impulse over the apex of the heart in the fifth space. Shock, thrill and enlargement of the heart were not noted; the sounds were of fair quality, and the second pulmonic sound was not accentuated. The abdomen was scaphoid; the liver and spleen were normal. Scars were present over both lower extremities. The reflexes were active. The thyroid gland was barely palpable.

Clinical Data.—The urine was normal. The blood count showed: 9,650 white blood cells, with 63 per cent polymorphonuclears, 33 per cent lymphocytes and 4 per cent large mononuclears; 4,700,000 red blood cells; 85 per cent hemoglobin. The tuberculin tests were negative. The blood sugar during fasting was 125.5 mg. The blood pressure was 80 systolic and 52 diastolic. The basal metabolic test was unsuccessful. A roentgenogram of the sinuses was negative.

Clinical Course.—The temperature remained between 98.6 and 100 F. On February 7 it reached 102 F. and declined from that day to the day of discharge to 100.4 F. The pulse remained rapid but not over 140. No extrasystoles were noted. There were no signs of congestive failure, and no fainting spells occurred. The rise in temperature was thought to be due to an abscess of the right lower premolar tooth and a pharyngitis. The child was taken home against advice. A diagnosis of paroxysmal tachycardia, complicated by a pharyngitis and abscess of the tooth, was made.

Electrocardiogram.—Figure 11, taken on January 25, in an attack, shows a regular auricular ventricular rate of 164. Definite P and T waves can be seen, and the P-R interval in the first lead is 0.12 second. In the second lead the

T waves are barely perceptible, but the P wave is very large and inverted; the P-R interval is 0.14 second. In the third lead the main deflection is semi-inverted; the P waves are inverted and unusually large. The rate is the same.

The impression was that the condition was paroxysmal auricular tachycardia with the aberrant pace-maker situated low down in the auricular musculature.

Subsequent History.—The child stayed home for two months and was then sent to a convalescent home, remaining there three months. She began then to complain of dyspnea, orthopnea, vomiting and epigastric pain, and was sent to a hospital, remaining there two weeks. After she had been home five days, the symptoms became so marked that she was admitted almost in collapse to the Mount

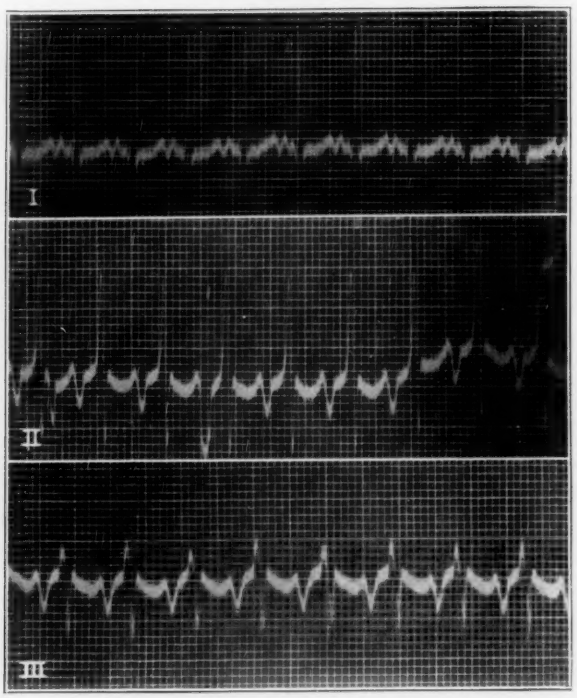

Fig. 11 (case 3).—Electrocardiogram taken on Jan. 25, 1929, in a case of auricular paroxysmal tachycardia; the ventricular rate is 164. This shows an absence of flutter waves and the sharply inverted P waves in the second and third leads.

Sinai Hospital on Aug. 29, 1928. A previous history similar to that given at the Jewish Hospital was obtained. A period of six months had elapsed since her admission to that institution.

On this admission the patient was slightly cyanotic, had a moist loose cough, headache, distress in the upper part of the abdomen, vomiting, attacks of fainting and dizziness and a feeling of impending death, tachycardia, dyspnea and orthopnea for two days and low grade rise in temperature.

Physical Examination.—On admission, petechiae or purpuric spots were not noted; the eyes, ears and nose were normal. The throat was red and injected; no tonsils were visible. The respirations were shallow but regular. The apex

of the heart was at the sixth interspace, 10 cm. from the midsternal line; the impulse was diffuse; the heart was enlarged to percussion to the left and downward and only slightly to the right. The right border was 3 cm. from the midsternal line in the second interspace, 5 cm. in the third interspace, 9 cm. in the fourth interspace and 12 cm. in the sixth interspace; the left border was 2 cm. from the midsternal line in the fourth interspace, 3 cm. in the fifth interspace and 4 cm. in the sixth interspace. The sounds were very rapid, and the rate about 200, and regular. At the apex the first sound was replaced by a musical murmur; the second sound was not heard because of the rapidity of the beat, and no diastolic murmur was heard. The second pulmonic sound was loud and the second aortic sound barely audible. At the base of the right lung, posteriorly, there were triangular areas of dulness and diminished breath sounds. The liver was tender and seemed to pulsate. There was no edema of the extremities.

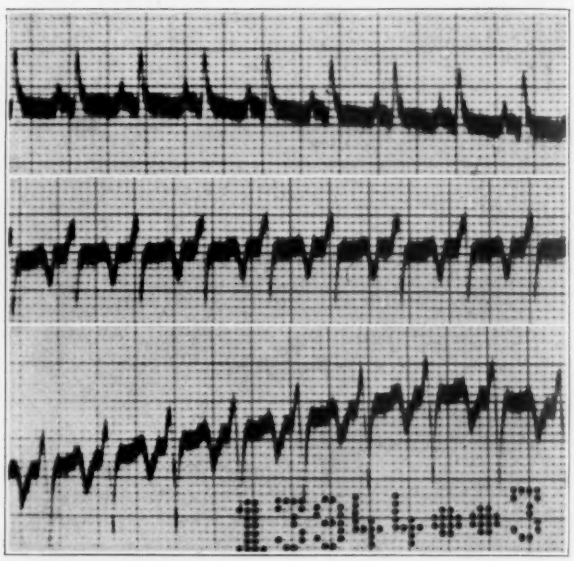

Fig. 12 (case 3).—Electrocardiogram taken on Aug. 28, 1929, seven months after figure 11. The ventricular rate is 182.

Roentgen Examination.—On August 30 the roentgenogram showed moderate increase in the lung markings due to congestion, and an azygous lobe was noted. The heart showed an enormous enlargement both to the right and the left with a mitral configuration.

Electrocardiogram.—Figure 12, taken on August 31, shows a tachycardia of ectopic auricular enlargement, with a rate of 182 per minute; the P waves are inverted and prominent in leads II and III. All main deflections are slurred. In the first lead the T is iso-electric. The Q-R-S is semi-inverted in leads II and III. There is marked left axis deviation.

Basal Metabolism.—On September 26, the basal metabolic rate was plus 11 per cent.

Electrocardiogram.—On December 6, the electrocardiogram showed a left axis deviation and an auricular fibrillation after digitalization.

Figure 13, taken on December 11, shows normal rhythm, with a rate of 120. There is marked left axis deviation. T_1 is of low voltage; P_2 and P_3 are inverted and large and widened. The P-R interval is 0.16 second. All main deflections are slurred.

The abnormal P_2 and P_3 in the electrocardiogram of December 11, showing the supposed normal rhythm at the rate of 120, are not easy to evaluate. It is possible that the abnormal P waves are due to marked organic changes in the auricular musculature. This case and these and subsequent records are being further studied.

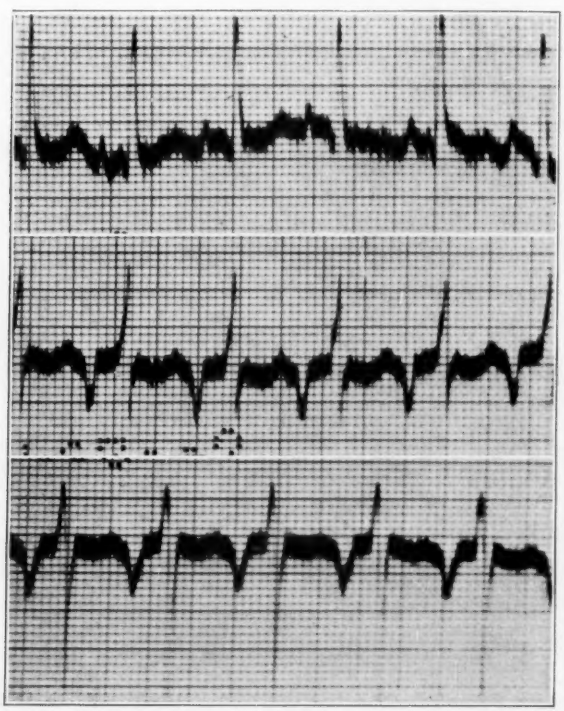

Fig. 13 (case 3).—Electrocardiogram taken on Dec. 11, 1928, showing normal sinus rhythm, rate 120, and left axis deviation. T_1 is of low voltage. P_2 and P_3 are sharply inverted and widened.

Clinical Data.—The blood pressure was normal. The Wassermann reaction was negative. The urine was normal. The Pirquet, Schick and Mantoux tests gave negative results. The blood count on August 31 showed: 80 per cent hemoglobin; 10,000 white blood cells with 58 per cent polymorphonuclears and 42 per cent lymphocytes. On October 17, there were 9,800 white blood cells with 62 per cent polymorphonuclears and 38 per cent lymphocytes. On November 14, the hemoglobin was 80 per cent.

Treatment.—Phlebotomy was done twice; tincture of digitalis was administered in large doses. Quinidine sulphate was tried, but it seemed to aggravate the condition; the liver would become more enlarged, signs of decompensation would increase, and large doses of digitalis would have to be used. On one occasion a

fibrillation as a result of the digitalis was noticed. Quinine urea hydrochloride was used intravenously once in an attempt to stop an attack of tachycardia, with no result. Later, compensation could be well maintained on 10 mm. of the tincture, three times a day.

The patient was referred to a convalescent home.

Comment.—The tachycardia in this case is a paroxysmal auricular tachycardia. The rates, 164 to 182, are lower than seen in cases 1, 2 and 4. The difference in rate in each attack, the absence of rhythmic movements of the iso-electric line, the definite P and T conformations, the large inverted P waves in the second and third leads, are all indicative of a tachycardia due to an ectopic focus low down in the auricular musculature.

Long before this child had any evidence of endocardial or myocardial disease—valvular defect, cardiac enlargement, signs of decompensation, etc.—she already had had attacks of a paroxysmal tachycardia with cerebral symptoms (syncope). The gradual progression of the organic deterioration with loss of cardiac reserve and subsequent endocarditis with cardiac decompensation are indicative of severe, active myocardial disease; the presence of a mitral stenosis and insufficiency practically makes certain that rheumatic fever is the cause. This case is particularly interesting because the paroxysmal tachycardia was a very early manifestation of rheumatic fever, and because of the occurrence of a transient auricular fibrillation between the attacks of paroxysmal auricular tachycardia.

CASE 4.—*History.*—B. K., a girl, aged 3 years, was admitted to the Jewish Hospital on April 23, 1930, and died on April 24, 1930. The chief complaints were listlessness and rapid heart rate, observed by the mother. The mother, aged 26, and the father, aged 33, were well. The mother had had two pregnancies; the first child was the patient, and the second a female child 2 days old. There had been no miscarriages or stillbirths. There was no history of tuberculosis, syphilis, cancer, renal, gastro-intestinal or nervous diseases.

The child was born at full term, with instrumental delivery. She weighed 7 pounds, 8 ounces (3,460 Gm.) at birth. Cyanosis, hemorrhages, desquamations or snuffles were not present. Feedings and developmental history were normal. The child had intussusception at 1 year, pertussis at 2 years, with convulsions during attacks of whooping cough, and tonsillitis. She had no other illnesses. A Schick test was found to be positive; antitoxin was given.

On March 24, a sore throat developed; the child was listless, refused to play, complained of dull aches, and was feverish. A physician could find nothing radically wrong. On April 1, she was reexamined because of listlessness, dull aches and pains. The parents were told that she had a very rapid heart rate. She was seen by one of us on April 11, and a diagnosis of paroxysmal tachycardia was made. She looked a little pale, and active systolic pulsations of the veins of the neck (Vorhofs-Pfropfung) were seen. The chest was clear. The heart was normal in size and shape, and the sounds were of good quality although very rapid; no murmurs were heard. There was no edema. The tonsils were slightly reddened and infected. The liver was two fingerbreadths below the costal margin. There were

no signs of cardiac decompensation. At this time the patient had already had her attack ten days before and was playful, happy and cheerful.

Electrocardiogram.—Figure 14, taken on April 11, shows a tachycardia with a ventricular rate of 246. Definite rhythmic movements of the string indicative of auricular flutter are seen in all leads. Figure 11 shows the base lines in leads I and II diagrammatically reconstructed. P and T waves cannot be differentiated. The prominent S wave in the first and second leads is a normal finding in children. There is little, if any, variation in the ventricular and auricular rate. An alternation is present in the first and second leads.

Oculobulbar pressure, change of position, vomiting and other vagal tests did not stop the attack nor did they influence the rate in the attack. Carotid sheath pressure,

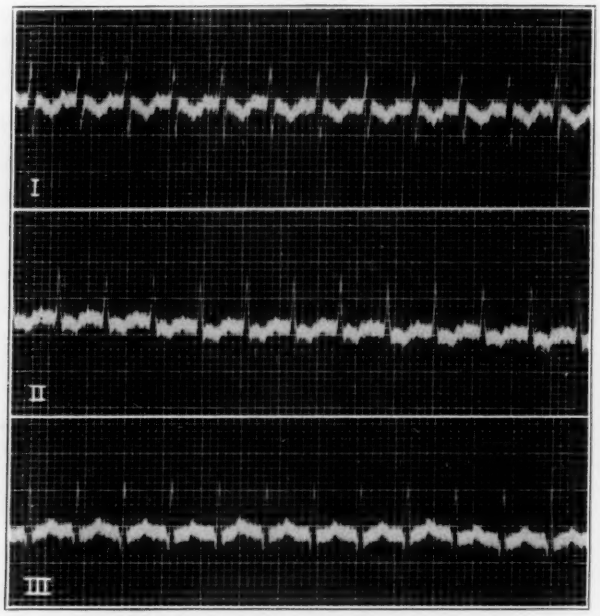

Fig. 14 (case 4).—Electrocardiogram showing auricular flutter. The auricular and ventricular rate is 246. Alternation of the ventricular complexes is seen best in the second lead.

however, caused an irregularity. The patient was given large doses of digitalis without any result. Five grains (0.32 Gm.) of quinine bisulphate had been given intravenously without any apparent effect; shortly after this the child had a maculopapular rash which disappeared after a day. Every method of procedure was tried but without avail. The attack continued, and in the last few days the patient began to complain again of abdominal pains; there was no vomiting or diarrhea. The liver was becoming larger. The parents finally consented to hospitalization. The child was admitted to the pediatric service of the Brooklyn Jewish Hospital on April 23.

Physical Examination.—On admission, the child appeared uncomfortable and pale, though well nourished. There was no cyanosis or jaundice, and only slight pallor. The scalp was normal. The pupils were equal and regular and reacted to

light. There was no mastoid tenderness or discharge from the ears, and no discharge from the nose or perforation of the septum. Dentition was fair. The pharynx was injected. The jugular veins were distended, and there were active venous pulsations. No cervical adenopathy was present. The lungs were resonant throughout; auscultation revealed normal breath sounds, but no râles. The apex impulse of the heart was felt; it was exceedingly rapid, 240 per minute. The rate and rhythm were regular. On percussion the heart was enlarged to the left, outside the midclavicular line. The sounds were of a pendulum character. There were no murmurs or thrills. The liver was felt three fingerbreadths below the costal margin and was enlarged. There were no other masses or tenderness. The back was normal. There was some edema of both feet, although no pitting on pressure. On the upper portion of the left side of the chest was a diffuse macular rash which did not disappear on pressure and was not tender. Some scratch marks were present.

The impression was that the condition was paroxysmal tachycardia, decompensation and toxic quinine rash.

Clinical Data.—The blood culture was negative. The blood count showed: hemoglobin, 67 per cent; red blood cells, 2,760,000; white blood cells, 9,600; polymorpho-

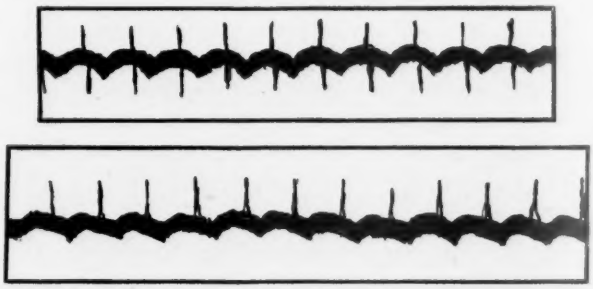

Fig. 15 (case 4).—Diagrammatic reconstruction of leads I and II (fig. 14) showing the regular continuous movements of the base line, not obstructed by the ventricular complexes.

nuclears, 43 per cent; lymphocytes, 48 per cent; large mononuclears and transitionals, 9 per cent. The respiratory rate was 56, and the temperature varied from 98.6 to 97.6 F. The weight was 36 pounds, 7 ounces (13,806 Gm.). The child vomited twice.

Treatment.—Ten grains (0.65 Gm.) of digitalis was given at 3 p. m.; the ice bag was applied to the precordium, and a soft diet prescribed.

At 3:45 a. m. on April 24, the next day, the patient suddenly became extremely cyanotic and expired in a few seconds.

Autopsy Report (by Dr. Max Lederer).—The body was that of a young white female child about 3 years of age. There were no external abnormalities. The body was well developed and well nourished. Postmortem lividity and rigidity were only slight.

The peritoneal cavity contained several hundred cubic centimeters of amber clear fluid. No fluid was seen in the pleural and pericardial cavities.

The trachea and esophagus appeared normal.

The thymus weighed 5 Gm., and showed fibrosis.

Microscopically, there were present relatively large remnants of thymic tissue. These were surrounded by extensive areas of fibrous tissue containing a moderate degree of round cell infiltration.

The pleural surfaces were smooth and glistening. The lungs crepitated well except the posterior portion of the right lower and middle lobes where the lung had an elastic consistency. On section, the lungs were pale and the cut surface exuded a moderate amount of frothy fluid. The right lower and middle lobes in their posterior position showed the reddish meaty appearance of atelectasis.

Fig. 16 (case 4).—Interstitial myocarditis in the healing state; × 100.

Microscopically, the lungs showed diffuse congestion with thickening of the alveolar walls and much exfoliation of the endothelium. Many of the alveoli contained Lenhartz cells. In portions of the lung the alveoli were collapsed.

The heart weighed 90 Gm. The pericardial surface was smooth and transparent. The heart was enlarged; it had a blunt apex and was tremendously widened transversely. The myocardium was very flabby and on section presented a silvery gray appearance. The left atrium was markedly dilated, and the wall was greatly thickened. The endocardium was smooth, but was wrinkled and corrugated. The mitral valves were normal. The left ventricle was greatly dilated while the wall showed only slight hypertrophy. At the apex of the left ventricle was an organized mural thrombus about 1.5 cm. in diameter. The right atrium and right ventricle

showed a moderate dilatation and hypertrophy. The foramen ovale and the ductus arteriosus were closed. The endocardium was smooth and transparent. The tricuspid pulmonary and aortic valves were normal.

Microscopically (figs. 16 and 17), the muscle fibers throughout were separated from one another by young loose connective tissue. A mild degree of round cell

Fig. 17 (case 4).—Interstitial myocarditis in the healing stage; × 500.

infiltration was noted, as well as fibroblasts in varying stages of development. The muscle fibers were long and thin, and the markings in many places were indistinct. In the ventricle was a thrombus which was continuous with the ventricular wall. It consisted of blood platelets and fibrin and showed beginning invasion of fibroblasts from the cardiac wall.

The liver weighed 440 Gm. The capsule was smooth. The organ had a mottled red and yellow color and a moderately firm consistency. On section, it presented the typical nutmeg appearance of chronic passive congestion. The gallbladder and biliary tract were normal. Microscopically, the liver was markedly congested. The capillaries were dilated. There were extensive areas of fatty degeneration around the central veins.

The gastro-intestinal tract was normal.

The spleen weighed 40 Gm. The surface was smooth. The consistence was moderately firm. On section, the organ presented the purplish color of congestion, with myriads of gray dots (lymphoid hyperplasia). Microscopically, the spleen was congested. There were many hemorrhages in the pulp.

The pancreas weighed 26 Gm. and appeared normal. Microscopically, it was congested.

The suprarenals weighed 4 Gm. each and appeared normal. Microscopically, they were congested. The cells of the cortex were the seat of a fatty degeneration.

The kidneys weighed 47 and 49 Gm. The capsule stripped easily, leaving a smooth congested surface. On section, the markings were normal. The ureters and bladder were normal. Microscopically, the glomeruli were congested. The Bowman space contained an exudate of plasma; the tubules were the seat of extensive hyaline degeneration.

The genito-urinary tract showed nothing abnormal.

The bone marrow was the seat of erythrogenic hyperplasia.

The anatomic diagnosis was (1) interstitial myocarditis in the healing stage, (2) intracardiac thrombus, (3) pulmonary atelectasis and chronic passive congestion, (4) chronic passive congestion of the liver, spleen, suprarenals and kidneys, (5) erythrogenic hyperplasia of the bone marrow, and (6) hydroperitoneum.

Clinical Impression.—The case showed clinically a paroxysmal tachycardia and pathologically interstitial myocarditis in the healing stage with dilatation of the heart. Associated findings were those of chronic passive congestion of the liver, spleen and kidneys and ascites.

Comment.—The electrocardiographic findings, i. e., the rhythmic movements of the iso-electric line in all leads, the high ventricular rate, the alternation and the length of the attack, make the diagnosis of a paroxysmal auricular flutter with a 1:1 rhythm.

The postmortem findings are of interest. Examination of the head was not allowed, and the possibility of a cerebral embolization from the thrombus in the ventricle could not be definitely ruled out. The acute cyanosis and death in a few seconds, however, speak for a ventricular fibrillation as the cause of death.

This patient had an infectious myocarditis with definite evidences of healing. The attacks began when the patient was convalescing from pertussis. The low grade infection of the upper respiratory tract, preceding the onset of the attack by one week, might have been a causal factor. It is surprising that in a child with definite myocardial disease a continuous rate of 246, lasting for about twenty-four days, caused so little signs of cardiac failure. Necropsy, however, showed signs of severe stasis in all organs.

COMMENT

The term paroxysmal tachycardia includes all forms of paroxysmal acceleration of the cardiac rate. The types of this arrhythmia encountered in children are paroxysmal auricular, ventricular, nodal tachycardia or paroxysmal auricular flutter, and all have their origin in an ectopic focus or ring. Of the forty cases described in the literature in children up to 15 years of age, one in a child with a progressive muscular dystrophy is a ventricular paroxysmal tachycardia; five are simple paroxysmal auricular tachycardia;[7] two, paroxysmal nodal tachycardia; twelve, paroxysmal auricular flutter, and in eighteen cases the type of paroxysmal tachycardia is undiagnosed because of the lack of mechanical registration. In only ten of this undiagnosed group are rates mentioned and in seven of these the rates were 200 or over. It is seen that the type of paroxysmal tachycardia most frequently encountered in children is paroxysmal auricular flutter.

A differential diagnosis between these types clinically is often impossible. The sudden onset and the sudden transition to a normal rhythm occur in all of these types and are, therefore, not differential diagnostic factors.

The conduction system in children is much more efficient than that in adults. Shookhoff and Taran [6] and others showed that both the P-R and the Q-R-S intervals in normal children up to and including 14 years of age are much shorter than the generally accepted normals for these intervals in adults. This explains why the occurrence of functional A-V block in flutter, in adults, is common and when present is diagnostic of that arrhythmia, and why in children 1 : 1 conduction in flutter is the rule. It also explains the frequent occurrence of temporary block in flutter in adults caused by reflex vagal stimulation, carotid sheath pressure and oculobulbar pressure, and the infrequency of this finding in children. If A-V block is present or an irregularity or slowing of the cardiac rate is caused by carotid sheath pressure in an attack of paroxysmal tachycardia, flutter can with assurance be diagnosed (Levine,[8] Wedd [9]). Our case 4 illustrates the latter point. While A-V block does occur in paroxysmal auricular tachycardia, it is extremely rare and it does not present the characteristics of block seen in flutter.

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7. Colgate and McCulloch's first case, diagnosed by them paroxysmal auricular tachycardia (Am. Heart J. **2**:160, 1926), Koplic's case diagnosed paroxysmal auricular tachycardia (Am. J. M. Sc. **154**:834, 1917) and Russell and Ellison's case, undiagnosed (Lancet **2**:546, 1927), are, we believe, auricular flutter with a 1 : 1 rhythm.

8. Levine, S. A.: The Clinical Recognition of the Various Types of Paroxysmal Rapid Heart Action, Boston M. & S. J. **184**:53, 1921.

9. Wedd, A. L.: Clinical Auricular Flutter, Ann. Clin. Med. **3**:69, 1924.

It is uncommon to see ventricular rates as high in paroxysmal, auricular, nodal or ventricular tachycardia as one sees in paroxysmal auricular flutter with 1 : 1 conduction. Lewis [10] expressed the belief that all auricular tachycardias with rates of over 200 are flutter. Wenckebach and Winterberg [11] believed that the higher the auricular rate, the more likely is the paroxysm to be flutter, although they themselves had observed a patient with a simple paroxysmal auricular tachycardia with a rate of 280. While higher rates, therefore, are more likely to indicate flutter, rate is not an absolute criterion.

In adults the occurrence of a 1 : 1 rhythm with flutter is of serious import; the patient becomes extremely ill and soon becomes decompensated. In children, owing to the shorter ventricular systole and greater efficiency of their heart muscle (Hecht [12]), signs of marked cardiac decompensation are uncommon and are seen only in attacks of long duration (case 4) or when widespread organic congenital or acquired disease exists.

Roentgenoscopy, as described by Hertz and Goodhart [13] and Holmes and White,[14] might be used for the diagnosis of flutter in adults by visualizing the auricular contractions, but we do not believe this procedure is of aid in children.

A definite diagnosis of the type of paroxysmal tachycardia by electrocardiographic studies is not always possible. If one were able to register the onset or the end of the attack, one might make a diagnosis. Such records, however, are rarely obtained. Paroxysmal nodal tachycardia can be differentiated by the abnormal relationship of the P wave to the Q-R-S complex and by the abnormal shape of the P wave, when these abnormalities are present. Paroxysmal ventricular tachycardia can be differentiated by the aberrant ventricular complexes. Aberrancy of ventricular complexes in auricular tachycardia or flutter in children is seldom seen owing to the better conductivity of their specific system, except when extensive myocardial disease is present and the specific system is severely damaged. In adults, when a 1 : 1 rhythm in flutter occurs, aberrance of the ventricular complex is the rule. A paroxysmal

10. Lewis, T.: Lectures on the Heart, New York, Paul B. Hoeber, Inc., 1915, p. 116.

11. Wenckebach, K. F., and Winterberg, H.: Unregelmässige Herztätigkeit, Leipzig, Wilhelm Engelmann, 1927, p. 489.

12. Hecht, H.: Die Mechanismus der Herzaktion im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **11**:324, 1913.

13. Hertz, A. F., and Goodhart, G. W.: The Speed Limit of the Human Heart, Quart. J. Med. **2**:213, 1908-1909.

14. Holmes, G. W., and White, P. D.: Auricular Flutter Detected by the Fluoroscope, J. A. M. A. **68**:844 (March 17) 1917.

tachycardia in which recurrent attacks are of approximately the same rate is most likely flutter (Lewis [15]). In case 2 the rate in repeated attacks was about 270 per minute. The rate in four attacks observed by Hutchinson and Parkinson [16] was about 245 in each attack. Alternation of the ventricles is more common in flutter (cases 2 and 4) (Mackenzie and Rothberger [17]).

Flutter is an auricular tachycardia dependent on a circuit movement in a hyperirritable ring of auricular musculature, and an expression of the continuous electrical activity of some portion of the auricular musculature is found in the contiguity and regularity of the auricular complexes. This is seen in the constantly moving string which does not rest for any length of time on the base line. The regularity of these auricular waves was emphasized by Lewis [18] who found maximum variations in cycles of the same curve to be usually less than 0.001 second. The constant regular movement of the iso-electric line is seen in cases 1, 2 and 4 and is absent in case 3.

While this finding is clearly described by Lewis,[19] it has not been used in the differential diagnosis of the paroxysmal tachycardias by those who have reported cases. We consider this a valuable point in the diagnosis of paroxysmal auricular flutter with a 1 : 1 rhythm.

To recapitulate, paroxysmal auricular flutter is differentiated from other types of paroxysmal tachycardia in children by: (1) the higher auricular ventricular rates (cases 1, 2 and 4); (2) the irregularity that may be caused by vagal stimulation (case 4); (3) the tendency of flutter to reestablish itself at approximately the original rate (case 2); (4) the greater tendency to alternation (cases 2 and 4); (5) the constant regular rhythmic movements of the string indicative of continuous auricular activity (cases 1, 2 and 4).

PATHOLOGY

Distinctive pathologic changes, either in the specific musculature or in the heart muscle proper, have not been found in paroxysmal tachycardia. Efforts to correlate pathologic changes in the auricle with flutter have been of no avail. That gross myocardial disease, like that produced by occlusion of a coronary vessel, may cause a paroxysmal tachycardia

15. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, London, Shaw & Sons, Ltd., 1925, p. 260.

16. Hutchinson, R., and Parkinson, J.: Paroxysmal Tachycardia in a Child, Brit. M. J. **1**:534, 1914.

17. Mackenzie, J., and Rothberger, C. J.: Herzkrankheiten, Berlin, J. Springer, 1923, p. 286.

18. Lewis, T.: Regularity of Clinical Auricular Flutter, Heart **7**:127, 1920.

19. Lewis (footnote 15, p. 260).

is well known (Lewis,[20] Smith[21]). Patients may, however, have extensive severe myocardial disease—degenerative, inflammatory, or based on gross coronary vessel disease—without ever having attacks of paroxysmal tachycardia. On the other hand, exhaustive pathologic studies on both the heart muscle and the specific system in patients who have suffered from this arrhythmia have revealed no abnormalities. The part that metabolic or chemical changes in the cell itself plays, changes due to either intrinsic or neurogenic disturbances, is not yet known.

In the cases in the literature, seven children had congenital cardiac disease (Poynton and Wyllie,[22] Amberg and Willius,[23] Werley,[5] Hoffman,[24] Faerber,[25] Russell and Ellison,[26] and Schuster and Paterson[27]), eleven showed evidence of myocarditis (Koplic,[28] two children, Essig,[2] Dressler and Löwy,[29] Franke and Weiner,[30] Sachs,[31] Willius and Amberg,[1] von Bernuth,[32] our cases 2, 3 and 4), three had endocarditis (Franke and Weiner,[30] Duken,[33] our case 3), two had cardiac decompensation (Faerber,[25] Sutherland[34]), one had progressive muscular

20. Lewis, T.: The Experimental Production of Paroxysmal Tachycardia and the Effect of Ligation of the Coronary Arteries, Heart **1**:98, 1909.

21. Smith, F. M.: Ligation of Coronary Artery with Electrocardiograph Study, Arch. Int. Med. **22**:8 (July) 1918.

22. Poynton, F. J., and Wyllie,, W. G.: Auricular Flutter in Infancy, Lancet **2**:371, 1926.

23. Amberg, S., and Willius, F. A.: Auricular Flutter in Congenital Heart Disease, Am. J. Dis. Child. **32**:99 (July) 1926.

24. Hoffman, A.: Die Paroxysmale Tachykardie, Weisbaden, J. F. Bergmann, 1900.

25. Faerber: Paroxysmale Tachykardie, Klin. Wchnschr. **5**:202, 1926.

26. Russell and Ellison: A Case of Prolonged Tachycardia, Lancet **2**:546, 1927.

27. Schuster, N. H., and Paterson, D.: Proc. Roy. Soc. Med. (Sect.. Dis. Child.) **17**:11, 1924.

28. Koplic, H.: Paroxysmal Tachycardia in Children, Am. J. M. Sc. **154**:834, 1917.

29. Dressler, W., and Löwy, M.: Ueber paroxysmale Tachykardie im Kindesalter, Med. Klin. **22**:1481 (Sept. 24) 1926.

30. Franke, W., and Weiner, R.: Die paroxysmale Tachykardie im Kindesalter, Ztschr. f. Kinderh. **46**:676, 1928.

31. Sachs, H.: Zur paroxysmale Tachykardie, Zentralbl. f. Herz- u. Gefässkr. **18**:65, 1926.

32. von Bernuth, F.: Ueber paroxysmale Tachykardie im Kindesalter, Ztschr. f. Kinderh. **47**:94, 1929.

33. Duken, J.: Profuse Lungenblutungen bei recidivierender Endocarditis und Polyarthritis im Kindesalter, Ztschr. f. Kinderh. **45**:333, 1928.

34. Sutherland, G. A.: The Heart in Early Life, London, H. Frowde, 1914, p. 80.

dystrophy (von Bernuth [32]), two had encephalitis (von Bernuth and von den Steiner [35]) and in one child the phrenic nerve had been resected because of a chronic purulent bronchiectasis (von Bernuth [32]). In six cases no pathologic data were given, and in eight there were no apparent evidences of cardiac disease.

In some cases (Willius and Amberg,[1] Sachs [31]), the constantly changing electrocardiographic findings were considered evidence of active myocardial disease. In other instances, a history of frequent attacks, gradually increasing signs of cardiac enlargement and diminution of cardiac reserve were considered evidences of myocardial disease.

While paroxysmal auricular flutter seems to be the most common type of paroxysmal tachycardia in children, it is apparent that the greater number of all types of paroxysmal acceleration of the heart rate in children reported are based on organic cardiac disease. Of the five cases of paroxysmal auricular tachycardia reported, at least two, our case 3 and Essig's [2] case, occurred in children with severe myocardial disease.

Paroxysmal auricular tachycardia in youth or in early middle life is considered, in the greater number of instances, a neurogenic disorder, no evidence of a pathologic process or disturbed function being found between attacks, while ventricular tachycardias have, in the greater number of instances, been associated with organic heart disease (Shookhoff [36]). Hoffman [24] associated organic heart disease with only one third of his series of cases of paroxysmal tachycardia. Flutter in adult life is nearly always based on a definite cardiac pathologic process, and occurs more frequently in later life as degenerative fibrotic changes increase.

In children this relationship of one or another type of paroxysmal tachycardia to organic or neurogenic disease does not seem to exist. Sinus arrhythmia is the only common type of arrhythmia in children. Extrasystoles are at least uncommon. In a series of two hundred and fifty-nine normal children between the ages of 5 and 14, only two older children with extrasystoles were observed (Shookhoff and Taran [6]). Lewis considered the occurrence of extrasystoles in children a great rarity. Bass [37] believed that transient myocardial disease is commonly the cause of extrasystoles in children. The occurrence of arrhythmias in children, due to hyperirritable ectopic foci, is more likely to be associated with myocardial disease.

ETIOLOGY

There is no specific etiology. A history of pertussis is frequently obtained in children suffering from paroxysmal tachycardia, and while

35. von Bernuth, F., and von den Steiner, R.: Paroxysmale Tachykardie ein Symptom von Encephalitis, Ztschr. f. Kinderh. **48**:686, 1930.

36. Shookhoff, C.: The Tachycardias, M. Clin. North America **11**:950, 1928.

37. Bass, M.: The Significance of Extrasystoles in Childhood, J. A. M. A. **86**:387 (Feb. 6) 1926.

this may be only coincidental, it occurs frequently enough to make note of it. In cases 2 and 4, the first attacks developed while the children were convalescing from pertussis. Willius and Amberg [1] commented on this possible relationship. Hauser,[38] Brick [39] and others described definite myocardial changes in pertussis.

Rothberger [40] expressed the belief that rheumatic fever is a causative factor in many cases of auricular flutter or tachycardia. Case 3 was undoubtedly one of endocarditis and myocarditis on a rheumatic basis, and one of the early symptoms of this involvement in this child was the occurrence of paroxysmal auricular tachycardia with syncopal attacks. The children with endocarditis and paroxysmal tachycardia were probably rheumatic.

Franke and Weiner's patient [30] had a positive Wassermann reaction, and they believed the tachycardia was the result of a syphilitic myocarditis.

Tonsillitis in children is very common, and it is, therefore, not striking to see infected tonsils mentioned in many of the case reports, but whether there is a causal relationship between tonsillitis and paroxysmal tachycardia we are not prepared to state. In case 2 the removal of the badly infected tonsils had no influence whatsoever on either the duration or the frequency of attacks subsequent to tonsillectomy.

Some cases, Franke and Weiner's first case,[30] our case 1, Koplic's cases 1 and 2,[28] Colgate and McCulloch's first case,[41] Sach's case,[31] and Dressler and Löwy's case,[29] and others, have a history of an acute infection, intestinal catarrh, tonsillitis, bronchitis or other respiratory infection, about two weeks preceding the onset of the first attack. It is possible that these infections supply the myocardial moment apparently necessary for the occurrence of these arrhythmias.

It seems to us that pertussis, rheumatism, syphilis or any other nonspecific infection which may cause low grade myocardial changes with early reactive fibrotic changes may be the myocardial disturbance necessary for the occurrence of these paroxysmal aberrant rhythms.

That extracardiac nervous mechanism disturbances play a part must be considered. Graber [42] reported a case of Hodgkin's disease in an

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38. Hauser, O.: Ueber Herzmuskelerkrankungen imfolge von Pertussis, Klin. Wchnschr. **48**:172, 1921.

39. Brick, M.: Ueber Herzveränderungen bei Pertussis, Virchows Arch. f. path. Anat. **212**:404, 1913.

40. Mackenzie and Rothberger (footnote 17, p. 276).

41. Colgate, C. E., and McCulloch, H.: Paroxysmal Tachycardia in Infancy, Am. Heart J. **2**:160, 1926.

42. Graber, V. C.: Paroxysms of Tachycardia Occurring in a Case of Hodgkin's Disease in Which the Vagus Nerves Were Degenerated by the Pressure of Enlarged Mediastinal Glands, Am. Heart J. **1**:564, 1926.

adult in whom the right and left vagi were involved by pressure of enlarged mediastinal glands, causing attacks of paroxysmal auricular tachycardia. Loss of vagal tone by administration of atropine in a patient predisposed to attacks of paroxysmal tachycardia often caused attacks (Galli [43]). In a girl in whom extrasystoles and paroxysmal tachycardia were prevalent, Kuré [44] could produce attacks by giving the girl sums in mental arithmetic. In the cases of encephalitis recorded by von Bernuth and von den Steiner,[35] it may be said that the paroxysmal attacks were caused by involvement of the vagal nucleus. The resection of the phrenic nerve might be considered the causative factor in another of von Bernuth's case.[32] It must not be forgotten, however, that in the last three mentioned children the acute infection in the first two, and the long standing pulmonary infection in the last, may have had some etiologic relationship by causing some parenchymal myocardial changes. Rothberger and Winterberg [45] showed that stimulating the sympathetic nerves when the heart muscle had previously been poisoned by barium chloride caused paroxysms of extrasystoles and other ectopic rhythms. Others have obtained similar results by using other myocardial poisons than barium chloride, i. e., chloroform.

It might well be that a combination of neurogenic and myocardial factors may account for the occurrence of these arrhythmias.

Wittgenstein [46] attempted to combine the occurrence of paroxysmal tachycardia with asthma and skin changes as evidence of an exudative diathesis. We have not observed any allergic phenomena in our cases, nor are they mentioned in any of the cases in the literature.

SYMPTOMATOLOGY

The symptoms of all types of paroxysmal tachycardia are much less pronounced in children than in adults. This is due not only to the more efficient conduction system, the greater resistance of their cardiac muscle to strain and the shorter systole, but to the absence in children of those neurogenic symptoms often seen in adults suffering from attacks of either the organic or neurogenic types.

There may be no symptoms. There may be symptoms of disturbed cerebral circulation only. Dizziness was an early symptom in Essig's

43. Galli, G.: Attacks of Paroxysmal Tachycardia Following Atropine, Heart **7**:111, 1920.

44. Kuré, K.: Psychisch ausgelöste paroxysmale kammer Tachysytolie, Deutsches Arch. f. klin. Med. **106**:33, 1912.

45. Rothberger, C. J., and Winterberg, H.: Ueber die experimentelle Erzeugung extrasystolischer ventrikulärer Tachykardie durch Acceleransreizung, Arch. f. d. ges. Physiol. **142**:461, 1911.

46. Wittgenstein: Exudative Diathese und vegetatives Nervensystem, Wien. Arch. f. inn. Med. **11**:417, 1925.

case,[2] while in our case 3 syncopal attacks called the parent's attention to the disorder. Barnes [47] described predominant cerebral symptomatology in paroxysmal tachycardia in adults. The symptoms may be reflex, gastro-intestinal, nausea, vomiting, loss of appetite, abdominal cramps, etc. The nausea and vomiting may be present only in the early part of longer attacks and then disappear and return later, owing to the more marked enlargement of the liver. Herringham's [48] patient complained of precordial oppression; this symptom is more common in adults. Symptoms of all degrees of severity of cardiac decompensation may be present.

Objectively, one may notice only a slight cyanosis or pallor. There may or may not be a slight increase in the respiration rate. In adults, paroxysmal dyspneas may occur. The Germans have described a peculiar "stosseweise Atmung," jerky breathing, particularly during sleep. A not uncommon sign, especially in the attacks with higher rates, is the rapid systolic pulsations of the jugular vein and bulb. This occurs at much lower rates in adults. It is due either to the simultaneous contraction of the auricle and ventricle, or to the greater amount of residual blood in the ventricle at the time of the auricular systole. While in adults this sign is seen only when there is decompensation, in children it may be present without any evident signs of decompensation (Dressler and Löwy [29]). The lungs are usually clear unless decompensation is present.

The heart may be of normal size in the attack. It not infrequently shows a slight bulging of the pulmonary curve, or it might be definitely enlarged. Smaller hearts than normal in the attack have not been seen in children. It seems to us that the size of the heart, particularly in the attack, is dependent on the amount of the underlying myocardial damage.

Usually the earliest sign of circulatory failure is enlargement of the liver. This may be present for some time before other symptoms of decompensation appear. There may be present all grades of cardiac failure.

Between attacks the patient may be perfectly well. When definite cardiac disease is present, the symptoms of that disease may be present in the intervening periods.

The duration of the attacks varies. In case 4, we believe, the duration of the attack is the longest on record—twenty-four days; in Herringham's [48] case the attack lasted thirteen days; in Hutchinson and Parkinson's [16] case, ten days; in Sach's [31] case, seven days, and in Franke and Weiner's [30] case, five days. Rosenbach expressed the belief that a long

47. Barnes, A. R.: Cerebral Manifestations of Paroxysmal Tachycardia, Am. J. M. Sc. **171**:489, 1926.

48. Herringham: Paroxysmal Tachycardia in a Child, Brit. M. J. **1**:144, 1887.

attack in itself is evidence of organic myocardial disease, while Christian [49] stated that long attacks may be the cause of myocardial degeneration.

PROGNOSIS

The paroxysmal tachycardias in children are most frequently dependent on definite disturbances in the myocardium, disturbances that are not necessarily gross and that in themselves may not cause cardiac insufficiency. The prognosis, therefore, of cases of paroxysmal tachycardia will depend, in the first place, on the degree and severity of the underlying myocardial disease; in the second place, even though there may be only minimal or no measurable amount of cardiac damage, on the frequency and the length of the attacks. The individual attacks in the great majority of instances are not fatal. Flutter, owing to the greater length of the individual attacks, may be of more serious import than auricular or nodal tachycardia.

Cardiac thrombosis and embolization are important possibilities. Ventricular thrombi were found in Franke and Weiner's [30] case, Sach's [31] case and our case 4. In Franke and Weiner's case both lower extremities were amputated because of embolization to both femoral arteries. Death from cardiac decompensation in the attack occurs, but most particularly in those cases with severe underlying organic cardiac disease. While patients may have most severe cardiac decompensation in the attack, it usually disappears rapidly after the attack is ended. It is almost unbelievable how great the ability of healthy muscle is to withstand great rates. Despite that, we must be guarded in our prognosis because of the possibility of unfavorable results through the occurrence of ventricular fibrillation (Wenckebach and Winterberg [50]).

Not enough children with arrhythmia have been studied for a long enough time to say definitely what the fate of such children is. The history occasionally obtained in adults of having had attacks since childhood shows that such children may live for many years. When we know why some people have attacks infrequently from childhood to adult life, why some have attacks frequently and of longer and shorter duration with severe symptomatology, while others may have only one attack and succumb, we shall understand more about the nature of this disease.

The common pathology, etiology and symptomatology in all types of paroxysmal tachycardia, auricular flutter, auricular fibrillation, paroxysmal auricular tachycardia, nodal and ventricular tachycardias in children

49. Christian, H. A.: Diagnosis and Treatment of Diseases of the Heart (Oxford Monographs on Diagnosis and Treatment), New York, Oxford University Press, 1929, vol. 3, p. 299.

50. Wenckebach and Winterberg (footnote 11, p. 491, case 1 B).

seem to strengthen the conception of Keating and Hajek,[51] Wolferth,[52] and others, of the close pathologicophysiologic relationship of these arrhythmias.

SUMMARY

1. Four cases of paroxysmal tachycardia in children are reported: three cases of paroxysmal auricular flutter with 1 : 1 conduction and one case of paroxysmal auricular tachycardia. The latter case showed evidence of severe rheumatic myocarditis and endocarditis, of which the occurrence of the paroxysmal tachycardia was one of the early, if not the first, symptom. Case 4 was that of a child who had one attack of paroxysmal auricular flutter with 1 : 1 rhythm. This child died rather suddenly after the attack had lasted twenty-four days. The necropsy report showed an infectious myocarditis in the healing stage.

2. Differential diagnosis between paroxysmal auricular flutter, the commonest type of paroxysmal acceleration of the heart rate in children, and the other types of paroxysmal tachycardia in children is discussed.

3. The pathology, etiology, prognosis and symptomatology of this disease are discussed.

4. The existence of a common pathology, etiology, prognosis and symptomatology for all types of paroxysmal tachycardia in children seems to strengthen the concept that they all have a common pathologico-physiologic basis.

5. Ectopic rhythms of all kinds in children are due, in part, to disease of the myocardium. The various types of paroxysmal tachycardia in children do not have the same relationship to neurogenic or organic causes as in adults: auricular neurogenic; ventricular organic.

6. Paroxysmal tachycardia must be considered in the differential diagnosis of obscure cerebral and gastro-intestinal manifestations in children.

51. Keating, J. H., and Hajek, J.: Auricular Flutter with a Report of Cases, Am. J. M. Sc. **164**:656, 1922.

52. Wolferth, C. C.: Intermittent (Impure) Auricular Flutter with Special Reference to Onsets and Offsets of Paroxysms and the Effect of Vagal Stimulation, Arch. Int. Med. **25**:42 (Jan.) 1925.

Case Reports

A RARE OSSEOUS DYSTROPHY (MORQUIO) *

HERMAN F. MEYER, M.D.
AND
JOSEPH BRENNEMANN, M.D.
CHICAGO

The excuse for reporting a single case lies, in this instance, in the twofold fact that it is unique in our experience, and that we have been able to find but one other apparently identical case in the literature.

For about eight years, or since he was 10 months old, a boy with a striking general deformity of the body has been in and out of our clinic at the Children's Memorial Hospital. From the start an object of curiosity, he became increasingly so as he grew older and the deformities became more evident (fig. 1). The early diagnosis of rickets—made even then with much reservation—was soon abandoned. His diet and hygiene and his general care by an intelligent mother had all been unexceptionable. Beyond the period of infancy the whole clinical picture was unlike anything that could be attributed to rickets. Free consultation together with sporadic attempts at a more intensive study of the condition and a search through the literature left us no nearer a solution as to the nature and classification of this strange multiple deformity.

While looking through the March, 1929, number of the *Archives de médecine des enfants,* one of us (Dr. Brennemann) came across a report by L. Morquio [1] of Montevideo, of four children out of five in one family all presenting an identical, widespread, osseous deformity.

* Submitted for publication, April 14, 1931.

* From the Children's Memorial Hospital.

* After this paper was submitted for publication our attention was directed by Dr. H. G. Ponchers, of Chicago, who had observed and studied a similar case, to a paper by Dr. Howard E. Ruggles, of San Francisco, entitled "Dwarfism Due to Disordered Epiphyseal Development," appearing in the January, 1931, issue of the American Journal of Roentgenology. Dr. Ruggles reported eight cases, five of which were familial, seen since 1918. His convincing photographs and descriptions leave no doubt that all of his cases, ours and Morquio's are identical in nature. He, too, could find no other report than Morquio's.

1. Morquio, L.: Sur une forme de dystrophie osseuse familiale, Arch. de méd. d. enfants **32**:129 (March) 1929.

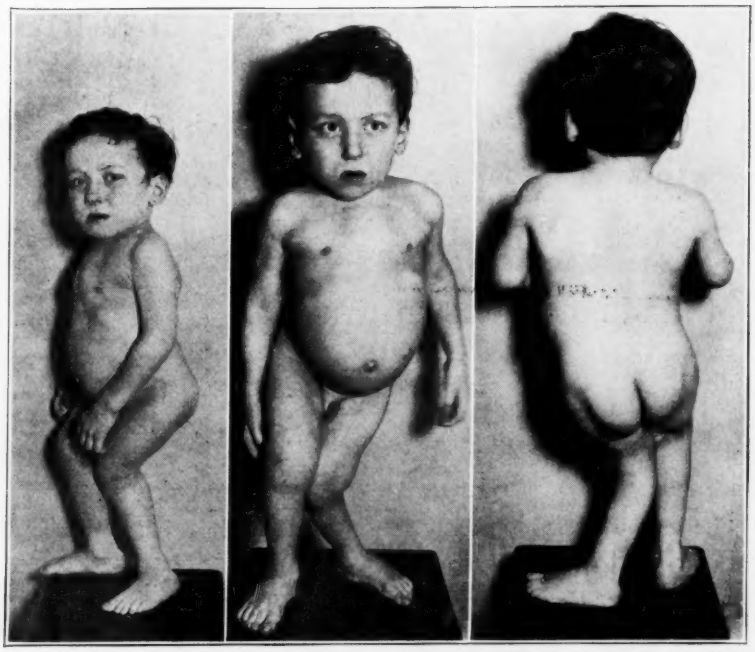

Fig. 1.—Photographs of our patient at 6½ years of age.

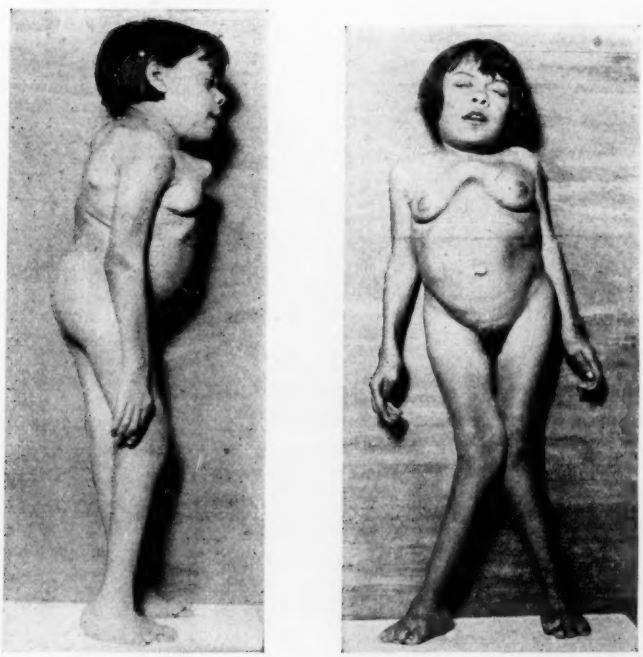

Fig. 2.—Photographic reprints of one of Morquio's patients, a girl, aged 14. (From the Archives de médecine des enfants, March, 1929, with the permission of Dr. Morquio.)

A glance at the photographs of two of these children, shown in that report (figs. 2 and 3), made it evident that they so clearly resembled our patient that there seemed little doubt that the essential pathologic changes were the same in all of them. This was further confirmed by a closer comparative study of Morquio's report and of our patient, both as to gross outward appearance and as to characteristic findings in roentgenograms of corresponding bones. Morquio, too, had searched the literature for reports of similar cases and had found

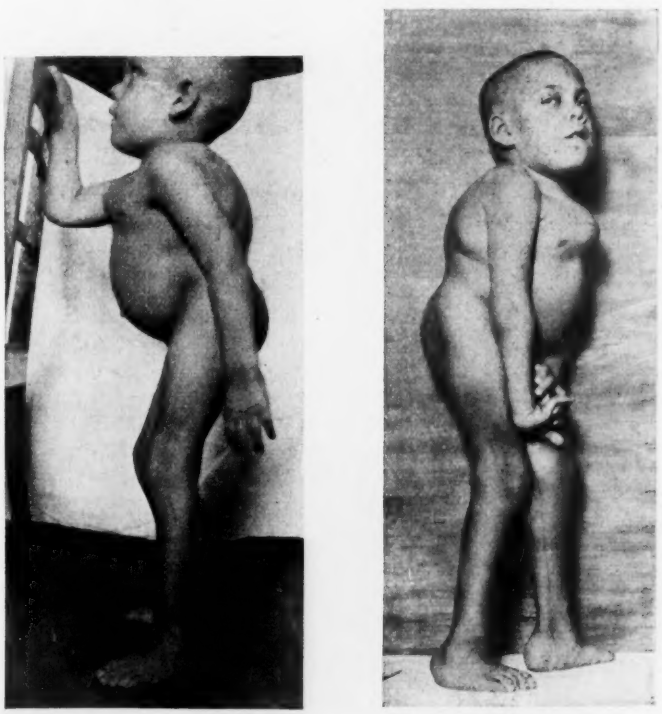

Fig. 3.—Photographic reprints of Morquio's other patient, a boy, aged 8 years. (From the Archives de médecine des enfants, March, 1929.)

none. One of the chief points of interest in presenting our case obviously lies in the question of whether it is identical in nature with those reported by Morquio. As the most convincing evidence is found in comparing the photographs of the children and the roentgenograms of the bones involved, it would seem desirable to reproduce such of Morquio's illustrations as are necessary to make an adequate comparison (figs. 2, 3 and 4).

Fig. 4.—Reprints of roentgenograms of M[illegible]io's patients showing [illegible]

REPORT OF CASE

J. V., a boy, was 8½ years old at the time this article was written. His father and mother were living and well. An older brother and two younger sisters were normal in every way. There had been no miscarriages. There was no history of any deformity in the three generations of both sides of the family with which the mother was familiar. The child was said to have been born three or four weeks beyond the obstetric calculation of the time of birth. The labor was of twelve hours' duration, and was terminated instrumentally. The baby weighed 9 pounds and 12 ounces (4,422.5 Gm.) at birth. He seemed normal to the mother in every way in early infancy. He was exclusively breast fed until 7 months of age, except that he had orange juice at 4 weeks and about 1 ounce (30 cc.) of tomato juice daily from the eighth week. When 7 months old he was taken to a physician, who said that he had a "tendency to rickets." He was then given 1 teaspoonful of plain and another of phosphorized cod liver oil daily until he was 10 months old, at which time he first came to our clinic. He was given 3 teaspoonfuls of cod liver oil daily after that, one half of which was phosphorized. Cereals and vegetables were given from the seventh month. He vomited quite frequently until 17 months old. He was said to have had pneumonia at 4 months of age and a second time at 15 months. He had measles when 2½ years old. He had had frequent infections of the respiratory tract, one of which led to an operation on the mastoid at 5 years of age.

When the boy was about 7 months old his mother noticed that he was short and was not growing as he should. She thought that this probably dated from about the fourth month. She also noticed at this time that the abdomen was getting larger. He could not hold up his head until the ninth month, and could not sit up until the fourteenth month. He began to crawl about the nineteenth month and to walk alone at 2 years and 9 months. His first teeth erupted at 9 months. He had always been very alert mentally, the mother stating that he "seemed brighter than my other children." He talked fairly well at 2 years of age.

The mother thought that the deformity of the left leg began rather suddenly when he was about 4 years old, and that the leg had gradually grown weaker and more deformed. She thought that his height and other deformities had remained about the same for several years. From our own observations we can state that practically all of his deformities were present, in kind, at the tenth month, when we saw him for the first time. They had naturally become more marked and more evident after he began to stand and walk. At 10 months the following note appeared, in substance, on the record in the outpatient department: "The infant is definitely malformed, the head is unusually large and somewhat square shaped, the bones are somewhat soft, the anterior fontanelle is normal. The neck is very short. The abdomen is quite large and the costal margins flare markedly. The arms and legs are shorter than normal for his age, the muscles are soft and flabby. He has two teeth." The tentative and rather hesitant diagnosis recorded of "rickets" and "chondrodystrophy (?)" doubtless influenced the observer in some respects that were not substantiated by closer study, such as, for example, in the matter of the length of the extremities. When the patient was a little over 11 months old, the following measurements were recorded: entire length of the body, 24½ inches (62.2 cm.); circumference of the head, 19 inches (48.2 cm.); circumference of the abdomen, 19 inches; circumference of the hips, 19 inches.

His weight at 1 year was 15 pounds (6,803.8 Gm.), and was said to be the same as at 4 months of age. Even at that time his length was 4 or 5 inches (10.16 or 12.7 cm.) less than one would expect in a child that weighed 9 pounds and 12 ounces at birth.

Fig. 4.—Reprints of roentgenograms of M[illegible] at 's patient[illegible]

The following description was recorded when the patient was 6½ years old (fig. 1): "The boy is strikingly malformed with a peculiar mixture of sturdy development of the head and shoulders, and a great distortion of the trunk and legs. He reminds one of the pictures one sees of a photograph of a normal head imposed on a caricature of a body. His relaxed, or functional, standing height is about ⅔ of what it should be for his age. The first glance suggests the hump back of an old thoracic Pott's disease. On closer inspection it becomes evident that the greatly diminished standing height is due to three main factors:

"1. There is practically no neck. The head seems to sit squarely on the thorax so that the chin rests on, and overlaps, the sternum. This is probably due wholly to an under development of the bodies of the cervical vertebrae.

"2. The trunk is greatly shortened due to an imperfect development of the spine. There is a well marked kyphosis of thorax. A general under-development, and consequent thinness of the bodies of all the vertebrae, is probably the greatest factor in the shortening of the spine and so of the whole trunk (fig. 7).

"3. His relaxed standing position is one of crouching. The hips are thrown back and up, the thighs are bent forward at nearly right angles to the spine, and the legs are flexed on the thigh at approximately the same angle. The left leg is furthermore in a position of extreme genu valgum (60° to 65°). The right leg is pushed forward and outward to accommodate the left leg. The feet are flat and everted, the left extremely so with a position nearly at right angles to the normal. The pelvis is tipped forward sharply and to the left. His normal, relaxed, standing height is determined by the left leg. When he straightens and stands on the right leg he increases his height by several inches. On walking his height sinks back to the level imposed by the functionally shortened left leg.

"His head is well shaped and of normal size, although it gives one the impression of being abnormally large. The face gives one an impression of unusual intelligence, though rather sober and thoughtful beyond his years for perhaps obvious reasons. The teeth are in good condition. The neck is not rigid, but there is some general limitation of motion. There is a slight adenoid facies.

"The thorax, in addition to the kyphosis already mentioned, has an increased anteroposterior diameter. This is probably due both to a lateral narrowing of the anterior portion of the thorax and to the abnormally short thoracic spine. These result in a 'pigeon-breast,' differing, however, from the usual appearance of that deformity in that the region of greatest prominence comes almost to a point over the middle of the sternum. The sternum is not only pushed forward, it is also bent forward on its long axis. This singular deformity was apparently even more marked in Morquio's patients.

"The abdomen is prominent and somewhat pendant. In all probability this is not due to a real so much as an apparent increase in size. The abnormal shortness of the spine, both above and below the diaphragm would, of necessity, push the normal sized abdomen forward and down. The abdominal walls are soft and yielding. The liver extends 4 cm. below the costal border. The spleen is not palpable.

"The shoulders are of normal width but appear abnormally large as compared with the rest of the body. The arms are of normal and equal length, but, naturally, give the appearance of unusual length inasmuch as they reach to the knees in the relaxed standing position. This is due both to the short spine and to the crouching position. The hands and fingers are long and soft.

"There is a slight general muscular weakness that may be due to the inactivity imposed by the skeletal deformities. The patellar reflexes are present. The plantar and abdominal reflexes could not be elicited. There are no pathologic reflexes.

"The genitalia appear normal.

"There has been an increasing difficulty in walking up to about six months ago. Since then there has been some improvement. There has never been any associated pain anywhere. The gait is that of extreme waddling like that of a duck ('comme un canard,' Morquio), or of a child with a bilateral congenital dislocation of the hip, except that it is exaggerated in one direction on account of the fact that one side is more deformed than the other."

His measurements at 7 years of age were as follows:

		Approximate Normal (Holt)
Circumference of the head.....	21 inches	20½ inches
Standing height	32 inches	36 inches
Sitting height	19½ inches	23 inches
Weight	31 pounds	50 pounds
Chest circumference	37½ inches	24 inches
Abdominal circumference	37½ inches	20 7/10 inches
Length of the right leg (actual)...	15½ inches	19 inches
Length of the left leg (actual).....	15 inches	19 inches
Length of the right arm (actual)..	15 inches	16 inches
Length of the left arm (actual)...	15 inches	16 inches

From these measurements it is evident that the child's weight was a little less than two thirds, and the height a little more than two thirds, of an approximate normal. The chest had approximately one-half, again, and the abdomen nearly twice the circumference of the normal for his age. The legs were about 4 inches short. The head and arms alone were of normal dimensions.

Laboratory studies showed: The urine was at all times normal. Examination of the blood showed: red cells, 4,856,000 per cubic millimeter; white cells, 9,400 per cubic millimeter; hemoglobin, 85 per cent. A differential count showed: polymorphonuclears, 60 per cent; mononuclears, 40 per cent. The coagulation time was 3½ minutes. Wassermann and Kahn tests of the blood gave negative results on two occasions. At 6½ years of age, chemical analysis of the blood showed: nonprotein nitrogen, 32; urea, 37; urea nitrogen, 17; uric acid, 2.1; creatinine, 1.3; phosphorus, 3.8; calcium, 10.8; sugar, 70 (all in milligrams per hundred cubic centimeters of blood). At 5½ years of age, the determination for calcium was 12.8, and for phosphorus, 4.3 mg. per hundred cubic centimeters of blood. The tuberculin, Pirquet and Mantoux tests gave negative results.

During the last eighteen months the child had shown marked improvement. He walked with alacrity, and when he walked rapidly there was more of a hop than a waddle. His face had become animated, and he seemed even brighter and more intelligent than before. He got along well in school. The improvement, however, was wholly functional—the deformity remained the same, and there was no apparent change in the roentgenograms of the bones. For the last five months he had been getting 90 drops of viosterol, 250 D (Meads) a day. We are not aware that his improvement was hastened in any way by this therapy. A determination of the blood calcium and phosphorus made at the end of this five month period, yielded 8.1 and 6.8 mg. per hundred cubic centimeters of blood, respectively.

As we have to deal with a widespread, symmetrical, osseous deformity, roentgenograms of the bones might be expected to give us the most exact information obtainable, in vivo, as to the essential underlying pathologic changes. Roentgenograms of the whole body were taken at the eleventh month and at the end of the second year; of the extremities at the age of 5 years and 2 months; a very full and detailed series of the whole body at 6 years and 4 months, and at 8 years; of

the hands and feet alone at 6½ years. All of these were submitted to Dr. P. C. Hodges, professor of roentgenology at the University of Chicago, who has given us the following interpretation:

Roentgenograms taken at 11 months of age showed (fig. 5): "There is definitely delayed epiphyseal development. The pelvic blades are small, the pubic rami absent, the centers for femoral heads are absent, those for the lower ends of the femur and upper ends of the tibiae are very small. In addition there is generalized decalcification of all the bones visualized, but with increased peripheral density."

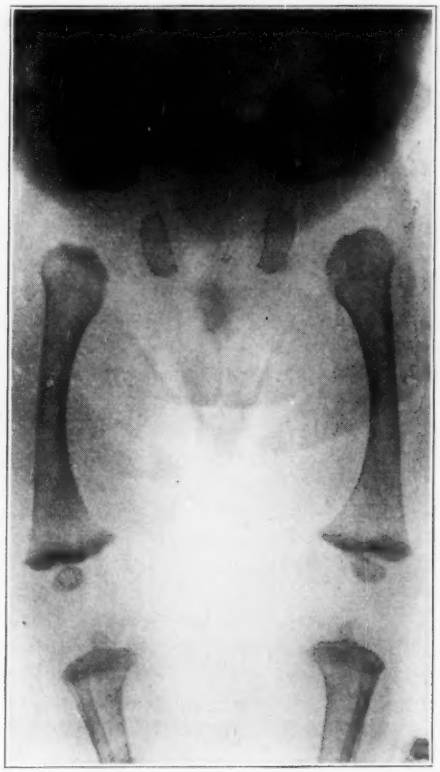

Fig. 5.—Roentgenogram of the pelvis and the bones of the legs of our patient when 11 months old.

No report was given on the films taken at the age of 2 years. There was no striking change in the pelvis as compared with the earlier films. There was noticed a definite change in the ends of the long bones of the legs. The upper ends of the femora appeared undeveloped, pointed and "mouse eaten"; the lower ends were of irregular density, giving an almost cystlike appearance.

Roentgenograms taken during the fifth and sixth years showed: "There is no striking abnormality at the elbows except delayed development of the epiphyses and generalized decalcification. The knees show frank lesions. The principal lesion appears to be at the end of the diaphysis close to the distal epiphysis of the femur, and in the proximal end of the diaphysis of the left tibia." In the films

taken at 6 years: "There is less epiphyseal development than in the normal child of nine months. The centers of ossification for the femoral heads have not appeared and there is practically no evidence of ossification in the acetabulum. The roughened upper ends of the femora are separated from the calcified parts of the acetabulum by clear spaces that are apparently totally non-calcified cartilage. The spine shows a definite under-development of vertebral bodies throughout. The terminal ends of the ribs are clubbed. The lungs are clear. The skull appears normal in all the films examined."

Roentgenograms of the hands and feet taken at 6 years and 4 months of age showed: "In the normal 5 year old hands there are well developed centers of ossification of six of the carpals. In this child at 6½ years there are only four centers and two of these are very small. The ankle films show gross underdevelopment of tarsals and metatarsals and there is a bulbous, cystic appearance to the lower ends of the tibial and fibular shafts" (figs. 6, 7, 8 and 9, taken at 8 years of age).

"Impression: The patient suffers from a generalized skeletal disease that has produced rarefaction of most of the bones visualized, has interfered grossly with the development of the epiphyses, and has produced cystlike deformities at the ends of certain of the long bones, notably the upper and lower ends of the femora, tibiae and fibulae. In the sense that the condition is an interference with the metamorphosis of cartilage into bone I should feel like classifying the condition as achondroplasia."

The following résumé from Morquio's paper shows how closely our patient and the foregoing description correspond with the cases that he has reported (figs. 2, 3 and 4):

"These manifestations are characterized by bony changes, without any pain, affecting the body, the vertebral column and the extremities, sparing the head and the face. They give rise to functional troubles, especially to those of motility, and to physical troubles that completely modify the harmony of the body. The deformities of the skeleton are generalized and absolutely symmetrical. In certain regions we find bony exuberance, as in the sternum, the vertebral column, the epiphyses of the shoulder, elbow, knees, etc. In others there is a retardation or absence of ossification, particularly in the palm, where one finds a complete void. The ligaments and peri-articular muscles are soft and relaxed, which gives a peculiar flaccidity to the joints, limited, however, in certain regions, as in the shoulders and elbows by bony deformities, while in others, such as in the hands and feet, the flaccidity is of extreme degree.

"As a consequence the whole body presents a marked deformity, characterized by a longitudinal shortening, and an anteroposterior deepening of the thorax, with the sternum projecting into a point, the whole thing forming a contrast with the extremities, which, though deformed, have normal dimensions, giving to the whole the appearance of children with Pott's disease, with an extensive cicatricial gibbus.

"The genu valgum, the flat foot, the malformation of the vertebral column, the weakness of the muscles and the tendons give rise to a difficult gait resembling that of a duck.

"The strength in the hands and feet is greatly diminished, without apparent muscular atrophy or changes in the electrical reactions.

"Intelligence is normal, proportional to age, with a face that is expressive and perfectly intelligent.

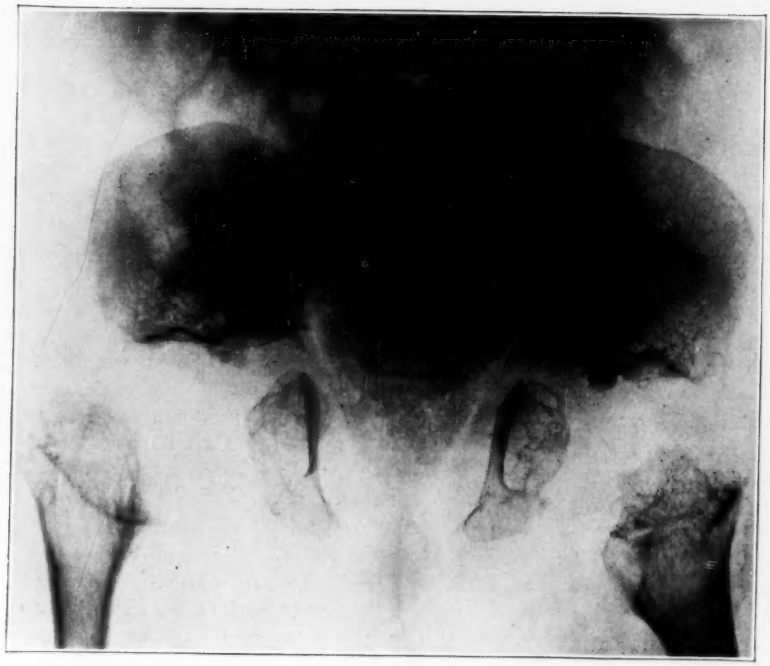

Fig. 6.—Roentgenogram of the pelvis of our patient when 8 years old.

Fig. 7.—Roentgenogram of the spine of our patient when 6½ years old.

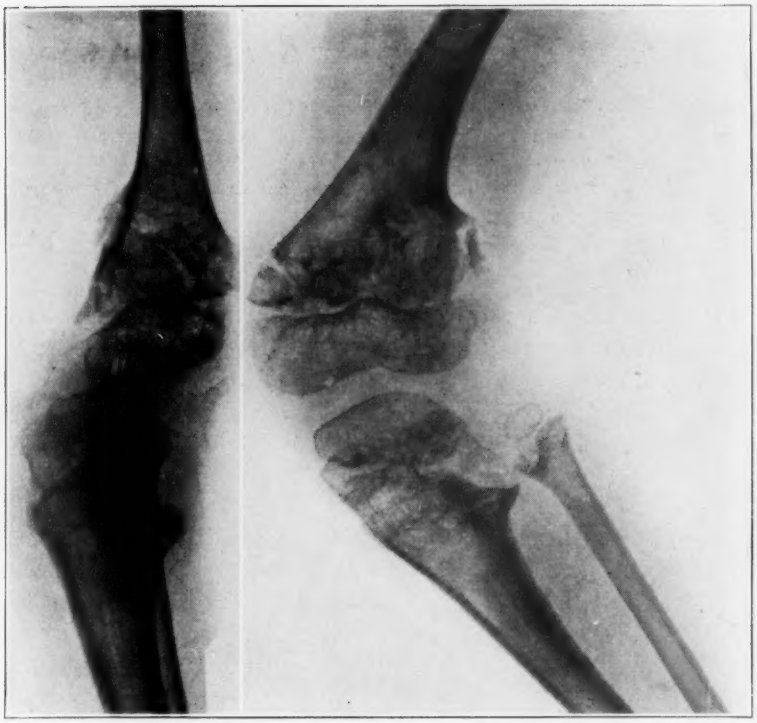

Fig. 8.—Roentgenogram of the knees of our patients at 8 years of age.

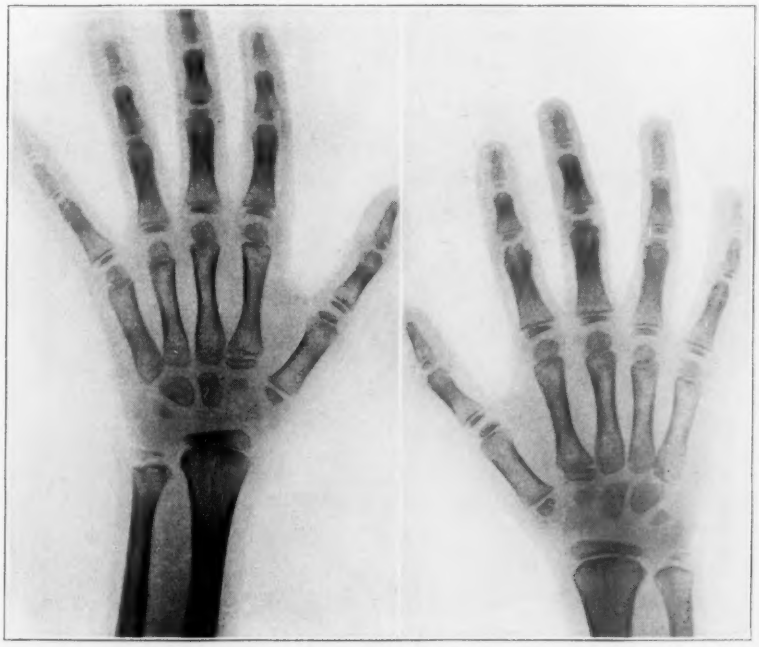

Fig. 9.—Roentgenogram of the hands of our patient at 6½ years of age, showing the lack of development of the carpal bones.

"Radiography visualizes the characteristics of the osseous changes, presenting a profound alteration in osteogenesis, explicable by the great diminution of the blood calcium. These changes consist in rarefactions, malformations, destructions, retardations and absences more or less complete in the extremities, affecting particularly the epiphyses of all the long bones, big and little."

COMMENT

From a comparison of respective descriptions, photographs and roentgenograms, it would seem to us that our patient and those of Morquio present an identical picture that is apparently one of extreme rarity. While there might be slight differences, they would seem rather of degree and of interpretation than of kind, and are no greater than those that exist between the two cases detailed by Morquio. The many points of resemblance in so many different parts of the skeleton, the exact correspondence in so many details of gross bodily deformity, would seem to point to a clinical entity that is sui generis and does not fit into any classification with which we have been able to acquaint ourselves. We hope in this report, by calling attention to this grossly easily recognizable clinical picture, to stimulate an interest that may disclose others of a like nature.

We have no theory to offer as to the underlying pathogenesis. It is interesting to note that the things that seemed to be of significance to Morquio are absent in our patient. The occurrence of four children so afflicted out of five in the same family reported by Morquio in itself establishes a familial tendency. This is wholly absent in our patient. The parents of Morquio's patients were cousins (*"cousins germains"*) and they in turn were descended from consanguineous parents, facts that he thinks should be duly considered. There was no consanguinity in the ascendants of our patient so far as can be known. Morquio, again, feels that the lowered blood calcium in the two patients detailed in his report, 5.2 mg. in the first patient of 14 years, and 4.5 mg. per hundred cubic centimeters of blood in the boy of 8 years, roughly one-half the normal amount, should be considered an important factor in the "trouble profond de l'osteogenese." Our patient, on the other hand, as we have seen, had normal calcium values of 12.8 mg. at 5 years and 10.8 mg. at 6½ years. The amount of cod liver oil given continuously to our patient may explain this discrepancy, but its total ineffectiveness in bringing about a change for the better would seem to absolve a lowered blood calcium as an essential factor in the causation of the skeletal changes. It is interesting to note the drop in calcium and rise in phosphorus after the ingestion of 90 drops of viosterol a day for five months. "The possible intervention of the nervous system, directly or through the intermediation of the endocrine glands" (Morquio) merely pushes the quest for an explanation into even more hazy territory.

We can agree with Dr. Hodges' view that the condition might be classified as achondroplasia, " in the sense that the condition is an interference with the metamorphosis of cartilage into bone." It must be emphasized, however, that achondroplasia in this sense is not the "achondroplasia," or chondrodystrophy, that has come into common usage to designate the most frequent type of dwarfism, a condition in which equally uniform, symmetrical and characteristic gross deformities are present, which in nearly all respects are the exact antithesis to those found in the present series. There are, moreover, changes that cannot be explained on the basis of achondroplasia alone.

SUMMARY

A report is presented of a child with a peculiar, gross, generalized, bodily deformity complex that is unique in our experience. We have, moreover, been able to find only one other report in the literature of an apparently identical condition. The essential pathologic change is evidently an osseous dystrophy involving practically the whole skeleton except the head, in which an achondroplasia is an important factor. We believe that the condition is a definite, uniform, clinical entity, that is, sui generis, and we hope that this view may be either confirmed, or refuted, in the experience of others.

707 Fullerton Avenue.

HEREDITARY ECTRODACTYLISM IN SIBLINGS*

IRWIN J. KLEIN, M.D.
BROOKLYN

Hereditary malformations of the extremities of various types in human beings have been described in the literature under such terms as syndactylism, polydactylism, brachydactylism, ectrodactylism, macrodactylism, hyperphalangism and hypophalangism. Other malformations of the extremities reported to be hereditary are such conditions as fragilitas osseum, cartilaginous exostosis and clubfoot. There is a vast literature replete with case reports and family histories of various inherited conditions.

Among constitutional anomalies that are inherited may be mentioned such conditions as deaf-mutism, chronic hereditary trophodermia, harelip and cleft palate, congenital cataract and dwarfism, color blindness and hemophilia. A broader conception of inheritances of systemic faults is found in Sir Archibald Garrod's "Inborn Errors of Metabolism," [1] in which one finds a fine discussion of such faults in body chemistry as albinism, alkaptonuria, cystinuria, hematoporphyria congenita and pentosuria.

Harvey Cushing [2] wrote an excellent monograph on symphallangism, in which there is absence or fusion of certain of the joints of the fingers, and has shown this to be hereditary. Murphy [3] made a study of syndactylism in five successive generations, and Perkoff [4] traced it through four generations. Weech [5] reported a case of combined acrocephalia and syndactylism occurring in mother and daughter. These cases support the view of Park and Powers that the combined malformations are evidence of defects in the germ plasm rather than the results of externally operating causes, such as bands and adhesions in

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* Submitted for publication, May 13, 1931.

* From the Pediatric Department of the Jewish Hospital.

* The records of this case are deposited in the Eugenics Record Office of the Carnegie Institute of Washington, at Cold Spring Harbor, L. I.

1. Garrod, A.: Inborn Errors of Metabolism, London, Oxford University Press, 1923.

2. Cushing, Harvey: Genetics, London **1**:90, 1915.

3. Murphy, D. P.: Five Successive Generations of Webbed-Finger Deformity, J. A. M. A. **84**:576 (Feb. 21) 1925.

4. Perkoff, D.: Brit. M. J. **2**:341 (Aug. 25) 1928.

5. Weech, A. A.: Bull. Johns Hopkins Hosp. **40**:73, 1927.

utero. So-called "lobster claw" deformity has been shown to be inherited, and excellent illustrations from casts of hands and feet with a number of case histories may be found in Coats' "Manual of Pathology." [6] In a study of over 1,000 cases of inherited anomalies, Macklin [7] concluded that there is evidence that the congenital malformations regarded by most observers as nonhereditary are in reality inherited and should be classed with other inherited defects. Lucker [8] mentioned a certain secluded village in which consanguineous marriages have been frequent, and here polydactylism is endemic. Collective polydactylism is reported by Luis G. de Linares [9] in a town near Madrid with a population of only 150. On the other hand, Yap and Pineda [10] reported tables showing hereditary deformities of the extremities, and stated that it is inconceivable that the determinants are invariably transmitted in some fixed form, for it has been shown that no two extremities or individuals had exactly identical deformities. The answer to this objection is that it is not necessary for two genetically identical individuals or characteristics of individuals to appear identically alike, because the phenotype depends not only on the genotype but also on the influence of the environment. Thus, two genetically identical plants, one raised on good and one on poor soil, may appear entirely different. Similarly, it is known that the two halves of the human body are not exact mirror images. This is explained on the basis of externally operating factors that modify the effect of the germ plasm. Thus, it is not necessary for an inherited deformity in the same family to be identically the same in appearance. However, in the case reported in this paper, the appearance of the deformities was identical in the two persons in whom it appeared.

The anomaly that is here presented is known as ectrodactylism or absence of fingers. This occurred in siblings of the same sex, with superficial and roentgenographic evidence of identical deformities. The antecedents for three generations were normal.

REPORT OF CASE

History.—A boy, aged 3 weeks, was brought by the mother to the dispensary for regulation of feeding. The child had had a normal birth. There was no cyanosis or convulsions at birth. The birth weight was 8 pounds (3.6 Kg.).

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6. Coats, J. A.: Manual of Pathology, ed. 3, New York, Longmans, Green & Company, 1895, fig. 16, p. 60.

7. Macklin, Madge Thurlow: Human Biol. **1**:382 (Sept.) 1929.

8. Lucker, F. C.: Monatschr. f. Geburtsh. u. Gynäk. **66**:327 (July) 1924.

9. de Linares, Luis G.: Collective Polydactylism in a Small Town, lecture quoted by Madrid correspondent, J. A. M. A. **94**:2080 (June 28) 1930.

10. Yap, E, and Pineda, E. V.: Philippine J. Sc. **20**:1 (Jan.) 1922.

Two other children were living and well. The first, a girl, 7 years of age, was normal in every way. The second, a boy, 5½ years of age, had a normal birth history and was normal except for deformity of both hands, as shall be described. The third child, the patient, was born with the identical deformity of both hands that his brother had.

The father and mother were living and well. There was no history of tuberculosis, diabetes or insanity in the family. Both were Spanish Jews, born in Asia Minor. They were related as uncle and niece, i. e., the father and the mother's father were half-brothers on their own father's side, though each had a different mother. There was no history of any other member in either family for three generations back having had any kind of deformity of the hands (fig. 1).

Physical Examination.—The turgor and color of the infant were good. There was no general adenopathy or craniotabes. The eyes, ears, nose, mouth and

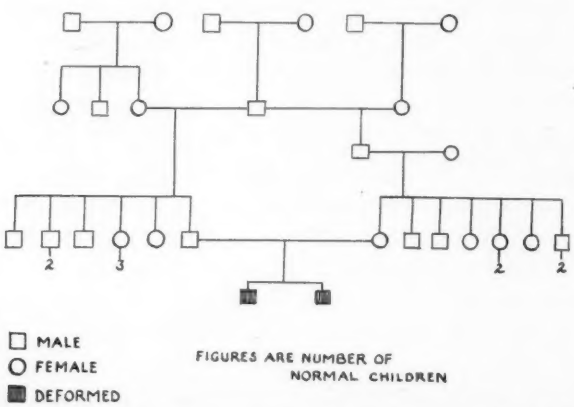

Fig. 1.—Family chart for three generations, showing absence of deformity.

pharynx were normal. The heart sounds were regular, rapid and of good quality. No murmurs were heard. The lungs and abdomen were normal. The reflexes were normal.

Each hand presented only three fingers. The thumb and small finger were normal. In place of the index, ring and middle fingers, a single digit was found, only the distal end of which appeared normal. The deformity was identical in both hands.

The second and third toes of the feet showed a slight degree of webbing at the base, but five normal toes were present on each foot. The brother, who was 5½ years old at the time, presented identical deformities of his hands and feet, and his physical examination revealed nothing else abnormal (figs. 2 and 3). The older boy could write easily and perform fine coordinating movements, such as buttoning his shirt.

The feet of both children and of the father and mother were roentgenographically negative. The hands of the father and mother were likewise roentgenographically negative. A roentgenogram of the patient's hand presented three metacarpal bones. The digits were markedly deformed and but three were

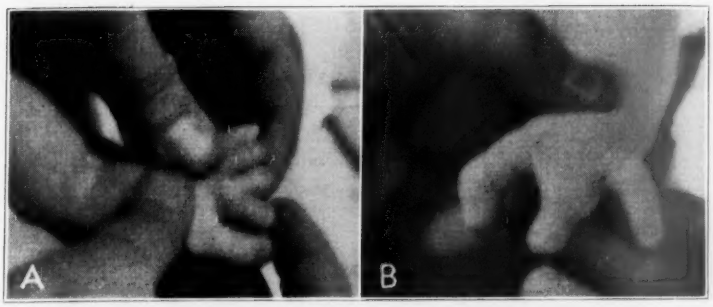

Fig. 2.—*A*, feet of an infant, aged 3 weeks; *B*, the hands.

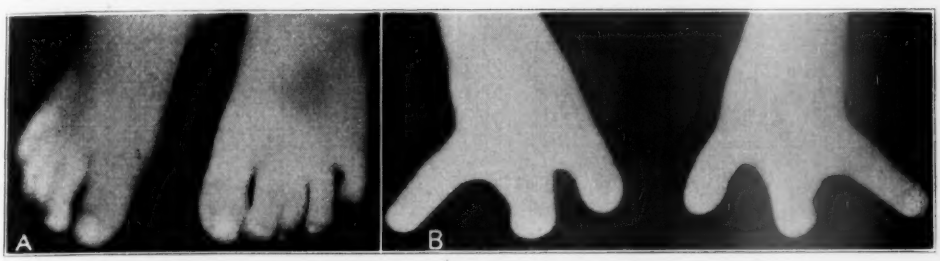

Fig. 3.—*A*, feet of a boy, aged 5½, a brother to the patient in figure 1; *B*, his hands.

Fig. 4.—Roentgenogram of the infant's hands shown in figure 2.

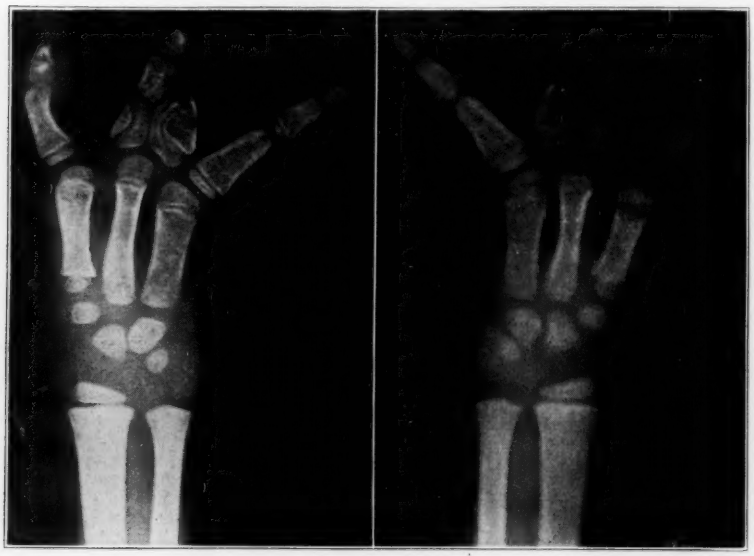

Fig. 5.—Roentgenogram of the boy's hands, shown in figure 3.

Fig. 6.—Roentgenogram of the father's normal hands.

present, with a rudimentary fourth which fused with the middle digit so that clinically it appeared as but one finger. No appreciable deformity of the metacarpals was present.

The roentgenograms of the older brother's hand presented the same deformity. The findings were bilateral in both brothers (figs. 4 and 5).

Wassermann and Kahn tests of the father and mother and both children gave negative results. All belonged to the same blood group (IV Moss or O International). The reason for typing the parents and children was that the possibility of illegitimacy was considered. There was nothing, however, in the clinical history or in the results of the typing to support this supposition.

The opinion was that surgical intervention was not feasible.

Fig. 7.—Roentgenogram of the mother's normal hands.

COMMENT

Inherited hand deformity is generally a dominant trait, and a dominant trait cannot appear in any child unless present in one or both parents. This is in contradistinction to a recessive trait, which may skip one or more generations and appear when neither parent shows the character.

Although the hand deformity is a dominant trait, Davenport [11] stated that "there are some cases of individuals who carry the gene for abnormal hand development who do not show any clear symptoms of abnormality in hand development. We think of these as the limiting

11. Davenport, C. B.: Personal communication, March 25, 1931.

or threshold conditions in which, despite an abnormal developmental tendency, such tendency does not express itself in frank abnormality."

As far as I have been able to trace, there is no previous family history as to any similar deformity, and the parents are likewise free from abnormality. Therefore, one of the possibilities to be considered is that a new mutation arose in the germ cells of either the father or the mother, and appeared in the sons. This case would then present a new mutation of what is usually considered a dominant trait.

Another possibility is that each of the parents carried the gene for the same anomaly as a recessive trait, because if two such germ cells united, the trait would be expressed. This possibility must be seriously considered, because the parents were blood relatives. In that event, it would be necessary to consider this case unusual, because here the deformity was inherited as a recessive trait, whereas hand deformities are usually inherited as dominant traits.

CHRONIC PARIETAL ENDOCARDITIS AND ACUTE ULCERATIVE THROMBO-ENDOCARDITIS WITH STREPTOCOCCUS VIRIDANS

IN A NINE MONTHS OLD INFANT *

ARTHUR EITEL BOYSEN, M.D.
BROWNWOOD, TEXAS

In comparison with the great number of the various heart conditions, the occurrence of parietal endocarditis is a rare entity. It is a condition that involves the endocardium of the wall of the heart without simultaneous valvulitis.

The oldest account of this condition is by Seitz,[1] in 1873, with a description of two cases, both in adults. In 1928, a summary of some of the reports of cases in the literature was given by Torres.[2]

Zuppinger,[3] in 1903, described two cases of endocardial thickening in children; one occurred at the age of 12 years following diphtheria, the other at the age of 10 years, in a tuberculous condition. Fischer [4] found the condition at necropsy in a boy of 5 years with congenital syphilis of the heart. Within that decade five other cases were reported, three following diphtheria and two following the opening of superficial ulcers. In 1928, Lawson and Palmer [5] described a case in which a child aged 21 months had an endocarditis without valvular changes, due to Streptococcus viridans.

In some of the cases the changes seem to be formed spontaneously but are thought to be due really to a blood stream infection or to circulating toxins. Baümler's [6] thorough investigation of several cases for the purpose of determining the etiology failed to elucidate the changes, and even now an uncertainty as to the cause continues to exist.

A cardiac hypertrophy accompanies this condition, and it is explained by Nauwerck [7] as an adjustment by the muscle for the ensuing parietal thickening, while Königer [8] regarded it as a vicarious hypertrophy due to the weakness of the heart musculature.

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* Submitted for publication, April 10, 1931.

1. Seitz, J.: Deutsches Arch f. klin. Med. **12**:143, 1873.
2. Torres: Mem. do Inst. Oswaldo Cruz **21**:219, 1928.
3. Zuppinger: Arch. f. Kinderh. **35**:381, 1902-1903.
4. Fischer, B.: Ueber hereditäre Syphilis des Herzens, München. med. Wchnschr. **51**:801, 1904.
5. Lawson, G. M., and Palmer, R. S.: New England J. Med. **199**:1205, 1928.
6. Baümler. C.: Deutsches Arch. f. klin. Med. **103**:1, 1911.
7. Nauwerck: Deutsches Arch. f. klin. Med. **33**:210, 1883.
8. Königer: Arb. a. d. path. Inst. zu Leipzig, 1903.

REPORT OF A CASE

History.—A colored girl, aged 9 months, was admitted to the Presbyterian Hospital, Chicago, on Oct. 18, 1930, and died nine and a half hours later. She was sent to the hospital because of swelling of the feet and legs and difficulty in breathing. She had been apparently normal in all respects until two days before admission, at which time the lower extremities became slightly swollen up to the level of the knees. The swelling became progressively worse. The skin became glossy and cold, but without pain. The child had a cold in the head at the time the swelling was first noticed, but she did not appear sick.

At birth, on Jan. 16, 1930, a midwife was in attendance and delivery was normal with no injuries. The pregnancy was normal and at term. The infant was breast fed for the first three months, and then feedings were changed to cow's milk, water and sugar. Later the mother had been giving four oatmeal feedings daily with milk. Elimination was encouraged weekly with castor oil and castoria. Cod liver oil and orange juice were begun the day the child became ill.

There was no history of any past illnesses of the child, nor had she been exposed to diphtheria, scarlet fever, measles, mumps, pertussis or any other infectious disease.

Two months before the child was born, the father, 36 years old, died of "inflammatory rheumatism" (mother's statement). The mother at 23 was in good health but was frail. Two brothers and one sister were living and well.

There was no history of tuberculosis, cancer, syphilis, epilepsy or kidney disease in the family.

Physical Examination.—Examination showed a well developed and nourished colored child in acute distress. She was very irritable, cried much and had swollen feet and legs. Dyspnea and hyperhidrosis were noticeably present.

The head was normal except for the slightly reddened and injected throat.

The symmetry of the chest was altered by the bulging over the left precordium. The resonance of the lungs was not impaired. Puerile breathing was present, yet a few fine expiratory râles were heard over both sides.

The apex beat was seen outside the nipple line, and percussion verified the presence of an enlarged heart. No murmurs were heard, but the sounds were not sharp. A palpably enlarged liver extended three fingerbreadths below the left costal border. The spleen was not felt. The upper extremities were normal, but the lower showed a sharply marked edema to the level of the knees. The skin was drawn tight, and the legs were cold and glossy. A subcutaneous edema extended to the waist.

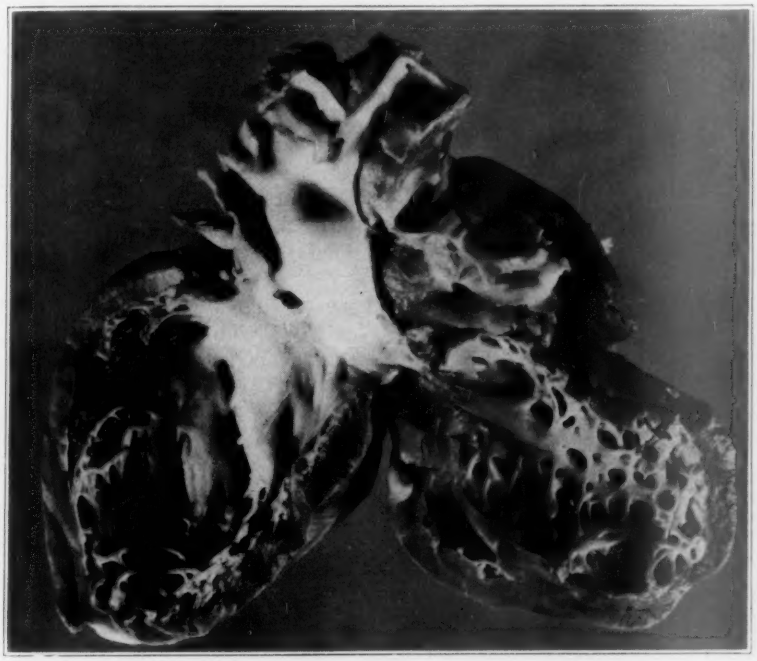
Vaginal smear was negative for the gonococcus. A roentgenogram showed a markedly enlarged heart. The mother's blood gave negative Wassermann and Kahn reactions.

Postmortem Examination (Dr. C. W. Apfelbach).—The body was that of a well nourished Negro infant weighing 13 pounds (5,896 Gm.). The abdomen was protuberant, and two deep transverse folds on the inner surface of the thighs indicated the overabundance of tissue. The left side of the chest over the cardiac area protruded 1 cm. more than the right side.

The gas-distended small bowel lay in a few centimeters of clear brown watery peritoneal fluid, and in the dependent portions, small veins and capillaries were engorged with blood.

The liver extended 3 cm. below the tip of the xiphoid process. It was mottled with red and golden yellow areas. The spleen was normally free and small.

When the chest was opened at least one third of the two thoracic cavities was occupied by the pericardial sac. The left lung was compressed in its lower half, dorsal to the sac. On each side there were a few cubic centimeters of watery fluid and in the distended pericardial sac there were at least 50 cc. of brown fluid. The chambers of the right side of the heart were markedly distended with blood. The apex was made up of the left ventricle. The base of the heart was wide, and the pulmonary artery and aorta were pushed upward and appeared as small tubes extending upward from the large base. Their circumferences were, however, within normal limits. There were three pulmonary cusps, and no obstruction in the pulmonary artery. The septum bulged into the cavity of the right ventricle. There was no malformation of the arch of the aorta.



Cross-section of the heart.

The ductus botalli was closed but from the aortic side a superficial pouch about 1 mm. deep extended toward the pulmonary artery. The cavity of the left ventricle was large and rounded, and the circumference of the aortic ring was 28 mm. and that of the mitral ring 43 mm. It was 64 mm. from the aortic ring to the apex of the ventricle. The maximum circumference of the left ventricle was 82 mm. The lining of the left ventricle was gray and opaque, and the maximum change was at the septum near the base, but everywhere the thickened endocardium could be distinguished from the underlying grayish-red myocardium as a membrane from 0.5 to 1 mm. thick. The majority of trabeculae carneae were grayish-pink threads less than 1 mm. in diameter, and the largest ones were 3 and 4 mm. in diameter. Papillary muscles were attached to the wall of the heart, halfway between the base and the apex, and their maximum diameter was only 7 mm.

A grayish-red to purple thrombus was attached to the lining of the heart in a place 3 cm. vertically to 2 cm. from side to side. This was in the front wall and began 1 cm. below the left aortic cusp. The cusps were equal in size and the width was approximately from 9 to 10 mm. They were flexible, and the coverings were smooth. The mitral leaflets had the normal shape. At the free margin of the posterior cusp, there was one region about 7 mm. long where the weblike free margin was replaced by a translucent glistening region from 1 to 1.5 mm. in diameter and several millimeters wide. The covering of the cusp and the covering of this enlarged free margin appeared to be continuous. The margin of the widest portion of the anterior mitral leaflet was slightly enlarged in a similar way. The lining of the left auricle was gray and opaque. There was no obstruction to the pulmonary veins. The auricular appendage was empty. The pulmonic ring was 34 mm. in circumference and the tricuspid, 55 mm. The lining of the right ventricle was thin, transparent and smooth. No alterations were present in the coverings of the tricuspid leaflets or pulmonary cusps.

No changes of the lining of the aorta, bronchi, esophagus, iliac veins or arteries, renal veins and arteries, common bile duct, gallbladder, stomach, bowel or urinary bladder were present.

In surfaces made by sectioning the liver, there were bright orange-yellow spots in almost every lobule. The central veins were small, and the central portion of the lobule was the part that was yellow.

The spleen was moderately firm, the capsule slightly wrinkled and the pulp was soft and bloody.

Histologic examination showed that at the junction of the endocardium (which was thickened by young fibrous connective tissue) with the myocardium there were extensive infiltrations of lymphocytes. The septums of the myocardium, especially near the endocardium, were abundant and thicker than normal.

The bacteriologic study of the pleural fluid and the peritoneal fluid gave no growth on blood agar (either aerobic or anaerobic) and ascitic fluid broth. A smear of the peritoneal fluid showed a few endothelial cells and occasional long slender gram-negative rods.

Culture of the material from the thrombus showed Streptococcus viridans.

The anatomic diagnosis was: chronic and acute parietal endocarditis of the left ventricle, dilatation of the cavity of the left ventricle, hypertrophy of the wall of the left ventricle, distention of the right ventricle with postmortem clotted blood, ascites and bilateral hydrothorax, compression atelectasis of the left lung and extensive fatty changes of the liver.

This is a case of chronic parietal endocarditis, according to the literature—a condition the etiology of which has never been explained. It is thought by some to be due to overwork at a much earlier period. The vegetation that was present in the left chamber was an ulcerative thrombo-endocarditis. It was a much more recent process than the parietal thickening and was due to Streptococcus viridans.

CEREBELLAR ABSCESS

DIAGNOSTIC DISCUSSION; SURGICAL INTERVENTION WITH COMPLETE RECOVERY *

SYDNEY NUSSBAUM, M.D.
Attending Pediatrician, Coney Island Hospital
AND
GEORGE WEBB, M.D.
Attending Surgeon, Coney Island Hospital
BROOKLYN

Abscess of the cerebellum is a sequel of chronic suppuration of the ear in 80 per cent of the recorded cases, but rarely of acute suppuration. The route of transmission of the infection is either through the labyrinth or by the way of the sigmoid sinus. The symptoms and signs are those of abscess of the brain, pain, headache, vomiting, fever, slow pulse, prostration, choked disk and yawning. In addition to these, there are the focal symptoms and signs, nystagmus, vertigo, disturbances of equilibrium, loss of the sense of position, past pointing, adiadokokinesis and speech disturbances.

Eagleton reported 50 per cent recovery in a series of these cases. Ten per cent recovery has been the general experience.

We consider the case to be described of interest because of the indefinite picture presented at the time of admission, the differential diagnostic discussions, the ultimate decision in favor of cerebellar abscess with a recommendation for surgical intervention and the rare complete recovery.

REPORT OF CASE

History.—L. C., a boy, aged 11 years, was admitted to the pediatric service on Sept. 5, 1930, with a history of dizziness and vomiting for the past week. The family history and the past personal history were essentially unimportant. He had never had an inflammation of the ear before this time.

The present illness began thirteen days before admission with pains in the left ear. Two days after this, spontaneous rupture of the tympanum took place, and a purulent discharge began which persisted to the time of admission. Two days after the onset of the discharge the patient complained of dizziness and extreme nausea followed by vomiting, particularly when he rotated his head toward the right. There were moderate headache and mild lethargy up to the time of admission. Two days before admission, the patient complained of diplopia.

Examination.—On admission, physical examination revealed a well nourished white boy, who responded readily to questions, but whose answers were not very clear; he had forgotten some of his recent symptoms. He lay constantly on his

* Submitted for publication, April 6, 1931.

left side, and when he was requested to turn to the right he objected strenuously, expressing his fear of a dizzy attack, which was brought on by this act. There was a slight purulent discharge in the left external auditory canal. The pupils were equal and responded to light and in accommodation. There was a slight left internal strabismus. A horizontal nystagmus was present, with the rapid component to the left. There was no stiffness of the neck. The heart, lungs and abdomen were normal. The deep reflexes were normal. The left abdominal reflex was absent. The pointing test, that is, finger-to-nose and finger-to-finger, showed inaccuracy with the left upper extremity. In attempting to place the left heel along the right tibia, he showed a similar condition in the left lower extremity. Inability to arrest one motor impulse and substitute for it one that was diametrically opposite, such as rotation of the hand in one direction and then in the other, was present on the left side (adiadokokinesis). These findings, indicating a lack of coordination of the musculature of the left side of the body, make up the syndrome termed hemiasynergia.

When the patient was requested to get out of bed, he was unable to balance his body with his eyes open; with his eyes shut and his heels and toes together, he almost fell to the floor (Romberg's sign). The gait was mildly ataxic. After the patient returned to bed, he suffered from a severe attack of dizziness and he vomited profusely.

Laboratory Data.—Urinalysis gave negative results. The white blood cells numbered 11,000, with a differential count of 61 per cent polymorphonuclears, 37 per cent lymphocytes, 1 per cent eosinophils and 1 per cent stab cells. Further examination of the blood showed: Wassermann and Kahn reactions, negative; dextrose, 60 mg. and chlorides, 680 mg. per hundred cubic centimeters. The spinal fluid poured out under moderately increased pressure when taps were performed on September 6 and 9. There were 4 cells per cubic millimeter in the first specimen and 100 cells in the second specimen. The globulin test gave a 1 + reaction on the latter specimen. Fehling's solution was reduced in both specimens. The Mantoux test gave negative results.

Roentgen study of the chest showed nothing abnormal. A roentgenogram of the left mastoid revealed chronic mastoiditis of the sclerosing type.

Examination of the eyeground showed nothing abnormal.

The following special tests were performed by the consulting otologists: The caloric test, consisting of syringing of the ears with hot or cold water, which normally causes an attack of dizziness and increased nystagmus, was performed in our case, and it produced no effect on the left side.

The watch test, in which the patient stated at what point from the ear the ticking of the watch was no longer heard, showed slight reduction in hearing power on the left side.

Schwabach's test, that is, the measurement of the time during which a series of tuning forks are heard by air conduction and bone conduction, gave normal results.

Diagnosis.—The foregoing findings brought into consideration the following possible diagnoses: acute labyrinthitis and cerebellar abscess or localized encephalitis in the region of the left cerebellar cortex, any of these being a complication of left purulent otitis media.

The presence of labyrinthitis was established by the defective hearing and the negative caloric test, but not in pure form. The presence of a cerebellar condition in addition had to be considered seriously. This was warranted by the presence of left hemiasynergia, ataxia, loss of equilibrium, a positive Romberg sign and a tendency to lie on the affected side (in pure labyrinthitis, the patient tends to lie on the sound side).

The question arose as to which form of cerebellar complication was present, cerebellar abscess or encephalitis. The absence of increased intracranial pressure, as was indicated by the normal blood pressure, normal optic disks and absence of projectile vomiting, severe headache and fever, was against the diagnosis of cerebellar abscess at this time. According to the Shilling method, in view of the absence of immature cells, interpretation of the blood count would indicate that there was no severe infection. It is true that certain well circumscribed cerebellar abscesses do not have some of these important signs, still so early in the course of the illness, some of these acute symptoms should be present. Encephalitis localized in the region of the left cerebellar cortex as a result of the transmission of infection or toxins from the adjacent inflamed labyrinth was the more acceptable diagnosis. This would account for the cerebellar symptoms and signs and for the absence of signs of intracranial pressure.

Our working diagnosis then read: acute purulent otitis media complicated by acute labyrinthitis and localized encephalitis in the region of the left cerebellar cortex.

Course.—The condition described persisted for thirteen days. On the eighteenth of September, the patient suddenly showed marked improvement, in that he was able to turn his head to the right without dizziness and vomiting. The nystagmus and hemiasynergia were lessened. This improvement became more apparent. The patient began to sit up, and he could stand with very little difficulty.

On September 25, there was a definite relapse. Again turning of the head produced dizziness, increased nystagmus, nausea and vomiting, but with greater intensity. There was no rise in temperature. The blood pressure was 102 systolic and 80 diastolic. Examination of the eyegrounds revealed signs of papilledema for the first time. There was slight diffuseness of the margins of the disks, with a pinkish-red hue, and engorgement of the blood vessels was more marked on the left side. Daily observation for the next three days revealed an increase of all these findings.

These changes were the first indications of increased intracranial pressure. The patient complained of severe headache. He became drowsy, and his answers to questions became more confused.

All those who were observing the case agreed that we were now dealing with a cerebellar abscess. The question arose as to whether the condition was originally an abscess or whether we had observed the formation of an abscess during the past four days. Most of us agreed that it was the latter. A surgeon was consulted and operative intervention advised.

Operation and Recovery.—On September 27, the patient was transferred to the surgical service of the hospital with the diagnosis of an abscess of the left hemisphere of the cerebellum.

The same evening operation was performed by Dr. Webb. The cerebellum was exposed through Cushing's cerebellar incision. The dura was incised radially over the bulging left hemisphere. The cerebellum was explored with a large calibered needle. Thick greenish pus was located at a depth of 1 cm. The needle tract was gently dilated by a closed hemostat, about 20 cc. of the pus being evacuated. A rubber catheter was then inserted into the cavity, and the cavity was gently irrigated with salt solution. A rubber tissue drain was placed into the abscess cavity; the dura was closed with fine chromic catgut, and then the entire wound was closed with a silkworm gut suture. The drain was brought out through a separate stab wound in a dependant position.

The convalescence was stormy for the first two days. The temperature and pulse rate rising to 104 F. and 100, respectively.

The rubber tissue drain was removed sixteen days later, when all discharge had ceased.

During the first three days after operation, the temperature rose, the sensorium was confused, and medical examination was impossible. On the fourth day and thereafter, the dizziness and nausea decreased, so that by the tenth day the patient was able to sit up and turn to the right without discomfort. The nystagmus, hemiasynergia and vertigo had disappeared. On the twenty-fourth day after operation, he was allowed out of bed, and he was discharged on the thirty-first day. All signs and symptoms had disappeared, except for slight residual papilledema.

COMMENT

The occurrence of cerebellar abscess in this case warranted the original impression of the existence of labyrinthitis, because of the frequent association of these two conditions. Suspicion of a localized condition in the region of the left hemisphere of the cerebellum was stated at the time of admission. At this time the condition was considered encephalitis resulting from infection from the adjacent inflamed labyrinth. When signs of intracranial pressure developed twenty days later, a diagnosis of cerebellar abscess was made. An unusual opportunity was had to observe this condition in its incipiency. The most remarkable feature was the rapidity and completeness of recovery following drainage of the abscess cavity. This indicates that the amount of cerebellar tissue destroyed was not great enough to affect the functioning of this part, so that recovery of the sensory and motor coordinating powers on the left side of the body was complete. This may have been the result of early diagnosis and early operation.

Progress in Pediatrics

THE COUNTESSE OF LINCOLNES NURSERIE

WITH A FOREWORD BY THOMAS LODGE; OXFORD, 1622

ERNEST CAULFIELD, M.D.

HARTFORD, CONN.

This small work of twenty some pages is not in a strict sense a contribution to the history of the diseases of children, but is concerned with the feeding of children and so might properly be classified as the second original work in English on a pediatric subject.* I can find no mention of the "Nurserie" in any work on pediatric or medical history. Many of the early writers devoted a few pages to the subject of maternal nursing, but this work is unique, not only in being entirely devoted to that subject, but in the method of presentation. The work is extremely rare. Even in 1752, it was described as a "very scarce tract," and although no very extensive search has been made in the course of these researches, but a single copy has been encountered, that in the British Museum.

Concerning Elizabeth Clinton, the authoress, little is known. She lived at a time when it was more important to record the life details of the male members of a family, however uninteresting, than of the female members, however important. There were at least six Countesses of Lincoln named Elizabeth. But the family tree is known, which helps to identify the authoress of the "Nurserie." Sir James Stumpe of Malmesbury, Wilts, had a daughter Elizabeth who married Sir Henry Knyvet (variously spelled Knevett, Knivit, etc.) of Charlton in Wiltshire, Knight. From this union there were at least two daughters; Elizabeth, "a lady of learning and virtue"; and Katherine, who married as her second husband Thomas Howard, Earl of Suffolk. Katherine possessed great beauty but questionable virtues; or as one historian stated: "Her beauty was remarkable, and I fear she made a bad use of her charms." About September, 1584, Elizabeth married Thomas Clinton, son of Henry, Earl of Lincoln. Thomas Clinton was born about 1571, was educated at Oxford and was summoned to Parliament in 1610. He succeeded as third Earl of Lincoln, on Sept. 29, 1616. There are a few extant notes concerning him that are worth mentioning, merely because they throw some light on the character of his wife.

* The first was the "Booke of Chyldren" by Thomas Phaer, first published in 1544. The only known copy of this edition is in the Huntington Library at San Marino, Calif.

One autobiographical account by Sir Henry Clinton follows:

Now to goe on, my brother Thomas, Earle of Lincolne, gave himself holly to trobles and sutes and broughte me and my hole estate in question. He sued me in all the cortes in England . . . also he gott all the despirate fellowes he

THE
COVNTESSE
OF LINCOLNES
NVRSERIE.

AT OXFORD,
Printed by IOHN LICHFIELD, and IAMES SHORT
Printers to the famous Universitie. 1622.

Fig. 1.—Title page of the copy in the British Museum.

could hear of, and caused them to walke 15 or 16 in a company, and to make divers and sundry assaultes upon me and my servantes; sumtimes he came himselfe with them, but alwayes when he had three to on odes. When he had thus tried all the corses that could be, he sodenly died, presently after Christmas, in the year 1619. The next day after, the Countis sent for me, and I went to her the day following, with home I was kindly entertayned, and agreed to have pease. The sommer following, I propounded to the Countis and yong Earle a fayre corce for

the division betwixt our toue lordships of Cristed and Tattershall, which was the chefe cause of difference and occasion of greatest mischefe, and the hardest thing to be desided betwixt us, . . .

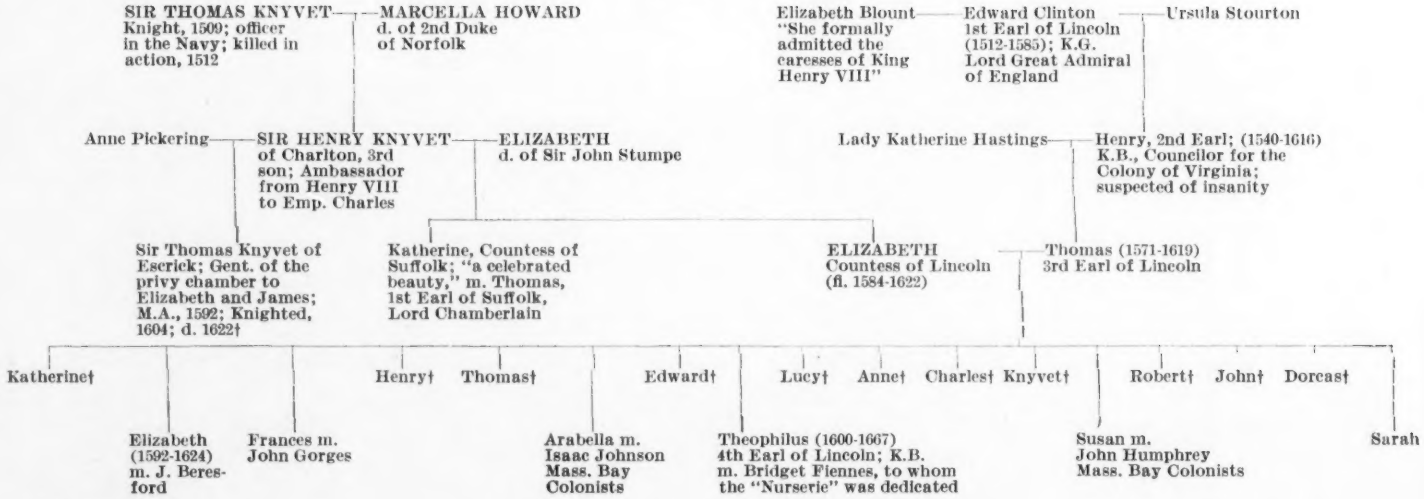
From what follows it appears that the countess, little given to disputes, settled the differences agreeably to all concerned.

From 1600 to 1612, this couple lived at Ponder's-End, Enfield, in an ancient mansion called Lincoln-House. Later they lived at Tattershall, Lincolnshire, where "The Right Honourable Thomas Earle of Lincolne departed this mortall life the 15th daye of January 1618 . . . and was buried in the chauncell of the church of Tattershall aforesaide." About 1620, the widow and three younger sons were living at Sempringham.

According to the countess there were eighteen children, though the records account for only seventeen, nine daughters and eight sons. Of these, eleven died "without issue." The exact ages of each at the time of death are not known, but many of them died in infancy. Theophilus, the only son to reach his majority, became the fourth Earl of Lincoln. It was to his wife, Bridget, that the "Nurserie" was dedicated, because she had the temerity to bring up her first child at the breast.

The Clinton family is historically interesting. Elizabeth, the eldest daughter, was a cause of concern. While on his deathbed, the Earl disinherited her because she married John Beresford, one of the family servants. The marriage of Frances to John Gorges, Esq., was one of the many intermarriages between these two families. Arbella (sometimes Arabella) married Isaac Johnson, a Puritan gentleman of Clipsham, Rutlandshire. Together with Winthrop, Dudley, Endecott and others, he was a prime mover in the Massachusetts Bay Company, and the flagship "Arbella" led the famous "Winthrop Fleet" to Salem, Mass., in 1630. Arbella died at Salem a few months after her arrival. Isaac removed to Shawmut, now Boston, which was settled under his personal supervision and where he died, the richest man in the colony, in September, 1630. Lady Susan Clinton married John Humphrey of Chaldon, who was chosen deputy governor of the Massachusetts company in 1629. He came to America in 1634, but in 1641, he decided to return to England. "He left two daughters of tender age in charge of a farmer near Lynn, who shamefully abused them, for which he was whipped, branded, and fined £20." When Humphrey declined the office, his place was filled by the election of Thomas Dudley, who was steward for Theophilus and managed the family estates. In the eighteenth century, a colonial governor of New York and a leader of the British forces in the War of the Revolution were members of the Clinton family, indirectly related to the countess. Thomas Knyvet, a stepbrother of the countess, was subsequently knighted. He apprehended

Family Tree


SIR THOMAS KNYVET
Knight, 1509; officer in the Navy; killed in action, 1512
MARCELLA HOWARD
d. of 2nd Duke of Norfolk
Elizabeth Blount
"She formally admitted the caresses of King Henry VIII"
Edward Clinton
1st Earl of Lincoln (1512-1585); K.G. Lord Great Admiral of England
Ursula Stourton
Anne Pickering
SIR HENRY KNYVET
of Charlton, 3rd son; Ambassador from Henry VIII to Emp. Charles
ELIZABETH
d. of Sir John Stumpe
Lady Katherine Hastings
Henry, 2nd Earl; (1540-1616) K.B., Councilor for the Colony of Virginia; suspected of insanity
Sir Thomas Knyvet of Escrick; Gent. of the privy chamber to Elizabeth and James; M.A., 1592; Knighted, 1604; d. 1622†
Katherine, Countess of Suffolk; "a celebrated beauty," m. Thomas, 1st Earl of Suffolk, Lord Chamberlain
ELIZABETH
Countess of Lincoln (fl. 1584-1622)
Thomas (1571-1619)
3rd Earl of Lincoln
Katherine†
Elizabeth (1592-1624) m. J. Beresford
Frances m. John Gorges
Henry†
Thomas†
Arabella m. Isaac Johnson Mass. Bay Colonists
Edward†
Theophilus (1600-1667) 4th Earl of Lincoln; K.B. m. Bridget Fiennes, to whom the "Nurserie" was dedicated
Lucy†
Anne†
Charles†
Knyvet†
Susan m. John Humphrey Mass. Bay Colonists
Robert†
John†
Dorcas†
Sarah

† Died without issue.

Guy Fawkes, who, early one November morning in 1605, was about to set a match to thirty-six barrels of gunpowder under the House of Lords.*

The countess is said to have long survived her noble consort, dying it is believed, in 1628. No other of her writings are known to exist.

After a brief dedication to Bridget, then Countess of Lincoln, the work gets off to an auspicious start with a foreword by Thomas Lodge. Forewords were rare at that time, at least in medical literature, and the countess did well to select Thomas Lodge to introduce her to the reading public.

The career of Thomas Lodge is of absorbing interest. A delightful account of him by Gosse is difficult to obtain. This, with an equally full account by Sidney Lee, makes one hesitate to relate the story of his life. But Lodge should be familiar to all students of medical history for he had few equals among medical men in attaining distinction in the world of letters.

Descended from an old Shropshire family, Lodge was born at West Ham, his father at one time having been Lord Mayor of London. He was educated at Merchant Taylor's School and in 1573 entered Trinity College, Oxford, from which he was graduated with a degree of Bachelor of Arts in 1577. Attracted to the study of law, he attended Lincoln's Inn in 1578, but soon turned from law to literature, for which he had a natural talent. His personal acquaintances numbered Greene, Daniel, Drayton and Lyly; he wrote prose for the booksellers and plays for the stage. But he was restless and unhappy. A careless way of life soon involved him in financial difficulties, and at this time he was probably well qualified to write "An Alarum Against Usurers."

"Afterwards falling from bookes to armes" he found the military life unattractive, and from 1584 to 1588 he undertook a series of voyages. It was the age of Hakluyt and men yearned to go down to the sea in ships, so Lodge set out on a buccaneering expedition to the Canaries with Captain Clarke. Even the "surges of many perillous seas" were not enough to occupy him and "to beguile the time with labour" he took to writing. After his return, he gave to the world his best known work, "Rosalynde, Euphues Golden Legacy." Though

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* In connection with Sir Thomas Knyvet, there is an interesting item that illustrates the manner in which the royal children were brought up in Stuart times. Early in life, they were placed in the homes of various noblemen, who were entrusted with the care and the education of the child. Thomas Knyvet was the guardian of Lady Mary, third daughter of James I. The following extract from an extant manuscript concerns her death at 18 months of age. "The Lady Mary died yesterday morning at Stanwell, the Lord Knevet's house. She had a burning fever for twenty-three days, and a continual rheum fell to her lungs, and putrefied there, which she had not strength to advoid."

influenced in his style by the euphusim of Lyly with its artificialities of construction and extravagant alliteration, the work is none the less of great importance. Scholars have debated its relative merits, but nearly all are agreed that Shakespeare was greatly indebted to this work for the plot and characters of "As You Like It."

The urge for travel found Lodge off again, this time to South America with Thomas Cavendish in 1591, and his verses composed on this voyage are notable for their bearing on Shakespeare's "Venus and Adonis." Next he tried historical romances, the chief one being "The Life and Death of William Longbeard, the most famous and witty English Traitor, Borne in the Citty of London. Accompanied with manye other most pleasant and prettie Histories. By T. L. of Lincoln's Inne, Gent. 1593."

In a more serious frame of mind, he traveled abroad to take up medicine. Graduating from Avignon in 1600, he soon returned to London and became successful as a practitioner. On Oct. 25, 1602, he received a degree of Doctor of Medicine at Oxford.

The year 1603 marked the death of Queen Elizabeth and the accession of James, but in the social history of the people, that year was more notable for an outbreak of the plague which had been more or less prevalent since the Black Death of 1348. Because Pepys and Defoe have left such dramatic accounts of the plague as it occurred in 1666, one is apt to believe that the other epidemics were less severe. But in proportion to the population, the plague in 1603 was just as devastating and mortal.

The revival of business and pleasure on the accession of James I was suddenly halted by the increase in deaths in the parish of Stepney. The epidemic rapidly spread through the city and beyond. It began in March, and by July the deaths each week were numbered in the hundreds. Funerals were so numerous that "three thousand mourners went as if trouping together, with rue and wormwood stuffed in their ears and nostrils, looking like so many boar's heads stuck with branches of rosemary." When morning came to the churchyards, there were bodies in heaps of tens and twenties. Beggars and gallants, husbands and wives, rich and poor found a common grave deprived of ceremony. The London lanes

> Did vomit out their undigested dead,
> Who by cartloads are carried to the grave.

The quality and all who could afford it fled the city. The clergy fled; the magistrates fled, and a good many of the doctors abandoned their patients to an ugly death. But Thomas Lodge was equal to the occasion. Unlike the great Sydenham under similar circumstances, he stuck to his post. He then contributed to the meager store of knowledge his

chief medical work: "Treatise of the Plague: containing the Nature, Signs, and Accidents of the Same, with certaine and absolute cure of the Fevers, Botches, and Carbuncles that raigne in these Times . . . London 1603."

The epidemic continued for a few years before the deaths from the plague resumed normal proportions for the times. Lodge became prosperous. About 1609, he was admitted licentiate of the College of Physicians. He then undertook some translations of the classics, notably Seneca. In 1614, he again traveled abroad, but a few years later, after his return, he was imprisoned for debt. He never published his other medical work, "The Poore Man's Talent."

Lodge lived at Low Laiton in Essex, but later as a physician in Warwick Lane, Lambert Hill, and lastly in Old Fish Street. He died in September, 1625, in the parish of St. Mary Magdelene, from the disease that most interested him and to which, by one of the ironies of fate, he had contributed a "certaine and absolute cure." Wood says that "he was as much cried up to his last for physic as he was in his younger days for his poetical fancy."

This lengthy digression concerning Lodge has been inserted not only because of his connection with the foreword, but because many different authorities following Wood have included "The Countess of Lincoln's Nursery" in the list of Lodge's works. There may be some internal evidence of which I am not aware, or Wood may have had access to some unpublished information, but the external evidence is against the theory that Lodge wrote the whole work. However, it is quite possible, in fact very probable, that Lodge corrected the manuscript before it went to press.

The foreword "to the courteous, chiefly most Christian, Reader" tells how one of the noblest and fairest ladies in the land was so ashamed to see so many mothers refusing to nurse their own children that "she made honour itself stoop" to tell them what was right. Lodge further informs us:

> Three things easily invite to read what to view is offered: Eminency or interest in the author, rarity in the handled matter, brevity in the quick dispatch. These three meet in this one. The author, so eminent in honour, thou canst hardly be anciently honourable, and not be interested in her honour's acquaintance, scarcely not alliance. Next for the rareness, a peculiar tract of this subject, is not in thine hands. Lastly, It is so brief, as I am persuaded, it smoothly gliding thee along in the reading, thy sorrow will be, it lands thee so soon.

The following quotations from the work itself are taken from an early nineteenth century reprint. The quaintness of the spelling has been sacrificed to make the reading easier, but the quotations are essentially as in the original.

(3)

dren in their own bosomes is Gods ordinance; They are very willful, or very ignorant, if they make a question of it. For it is proued sufficiently to be their dutie, both by Gods word, and also by his workes.

By his word it is proued, first by *Examples*, namely the example of *Eue*. For who suckled her sonnes Cain, Abel, Seth, &c. but her selfe? Which shee did not only of meere necessitie, because yet no other woman was created; but especially because shee was their mother, and so sawe it was her duty: and because shee had a true naturall affection, which moved her to doe it gladly. Next the example of *Sarah* the wife of *Abraham*; For shee both gaue her sonne *Isaac* suck, as doing the dutie commanded of God: And also tooke great comfort, and delight therein, as in a duty well pleasing to her selfe; whence shee spake of it, as of an action worthy to be named in her holy reioycing. Now if *Sarah*, so great a *Princesse*, did nurse her own childe, why should any of vs neglect to doe the like, except (which God forbid) we thinke scorne to follow her, whose daughters it is our glory to be, and which we Gen. 21. 7.

Fig. 2.—Specimen page.

Because it hath pleased God to bless me with many children, and so caused me to observe many things falling out to mothers, and to their children; I thought good to open my mind concerning a special matter belonging to all child bearing women, seriously to consider of; and to manifest my mind the better, even to write of this matter, so far as God will please to direct me; in sum, the matter I mean is, the duty of nursing, due by mothers to their own children.

In setting down whereof, I will, first, shew that every woman ought to nurse her own child; and secondly, I will endeavor to answer such objections, as are used to be cast out against this duty, to disgrace the same.

It was easy enough for her ladyship to prove that every woman ought to nurse her own child. The proof consisted merely in calling attention to the Almighty's revealed ordinance that women should do so. Believing this, what a troubled conscience must any woman have who should neglect that duty. She who did not believe it or who did not want to believe it was either very wilful or very ignorant. For the ordinance was proved "both by God's word and also by his works."

Elizabeth consulted the family Bible for examples of true womanhood. First there was Eve. "For who suckled her sons Cain, Abel, Seth &c but herself." Not only was there no provision for a wetnurse in the immediate neighborhood of the Garden of Eden, but mother Eve had a "true natural affection, which moved her to do it gladly." Secondly, there was Sarah, the wife of Abraham. She was not only very old "and so might have excused herself" but also she was "more able to hire a nurse than any of us."

After more biblical examples, the authoress turns for proof to the commands and works of the Creator. The first precept "which willith the younger women to marry, and to bear children, that is, not only to bear them in the womb, and to bring them forth, but also to bear them on their knee, in their arms, and at their breasts; . . . is numbered as the first of the good works, for which godly women should be well reported of." In the second precept, the countess rises to literary heights as her logic becomes less convincing: "I pray you, who, that judges aright, doth not hold the suckling of her own child the part of a true mother, of an honest mother, of a just mother, of a sincere mother, of a mother worthy of love, of a mother deserving good report, of a virtuous mother, of a mother winning praise for it? All this is assented to by any of good understanding." One nods assent and reads on to the list of works that she selects to prove her thesis.

The first is that dry breasts were a manifestation of a terrible judgment passed on the individual for her past sins. Inability was not an excuse but a confession of wickedness. Times have changed since James the first! Those who were blessed with good health and a plentiful supply of milk and who still refused to do their duty were "more savage than the dragons, and as cruel to their little ones as the ostridges."

Dragons and ostriches reminded the good countess of the other animals. Nowhere in nature had she observed that the young were brought forth by one dam and brought up by another. But reasoning from comparative physiology was too far beneath her dignity. She thought that intelligent women "should be shamed to be put to school to learn good nature of the unreasonable creature."

In the further development of her thesis, her ladyship, having completed the proofs in its favor, turns to answer all objections. I shall present only the second objection and her answer, for it is heard in this day as well:

> Secondly it is objected, that it is troublesome; that it is noisome to one's cloathes, that it makes one look old, &c. All such reasons are uncomely and unchristian to be objected, and therefore unworthy to be answered; they argue unmotherly affection, idleness, desire to have liberty to gad from home, pride, foolish fineness, lust, wantoness, and the like evils.

The countess was convinced of the soundness of her own arguments. But not a single one of them occurred to her in her younger days. She had eighteen children and every one of them was sent out to a wetnurse. Well she might give advice at a time when her husband was dead and when she was approaching an age in which she was in no danger of having another child. She selected the opportune time to expound her noble principles after having neglected nearly a score of golden opportunities to practice them. But there is a note of sincerity and appeal in her confession:

> I know and acknowledge that I should have done it, and not having done it, it was not for want of will in myself, but partly I was overruled by another's authority, and partly deceived by some ill counsel, and partly I had not so well considered of my duty in this motherly office, as since I did, when it was too late for me to put it in execution.

Elizabeth Clinton was not doing anything extraordinary in having wetnurses for her eighteen children. Throughout the ages there has always been a large proportion of mothers who would not nurse their babies, when given the opportunity to do otherwise. In one of his portrayals of human nature, Anthony Trollope described this trait with characteristic candor:

> Of course Lady Arabella could not suckle the young heir herself. Ladies Arabella never can. They are gifted with the powers of being mothers, but not nursing-mothers. Nature gives them bosoms for show, but not for use. So Lady Arabella had a wet-nurse.

Yet this practice cannot be entirely condemned as a frivolous fashion. Underlying some of it was the inability to nurse. It was the fashionable woman alone who could afford to hire a wetnurse. The infants of the lower classes got along the best they could with "teething" and "colic."

The rearing of children being a past duty in her life, why should the Countess of Lincoln have gone to all the trouble of proving by Scripture that it was a mother's duty to nurse her own child? Something unusual had happened. Her first grandchild had come into the world, and the child's mother, throwing fashion to the wind, had nursed the baby herself. This example of motherly affection within the family had probably come home to the dowager with the force of an unanswerable argument, and, in her old age, it very likely troubled her conscience.

Moreover, the results of her own experience with wetnurses gave the countess little cause to complain. True, of all the nurses she had employed for her eighteen children, she found only two who were thoroughly willing and careful. Nevertheless, of all the deaths in her family, she could attribute only one or two to the default of the nurses. Had she been fully aware of the general infant mortality of her time which could be attributed to the wetnursing system, she might have considered herself particularly fortunate and that her own singular experience was really an argument in favor of wetnursing.

Aside from her inconsistency, the countess had good reason to advocate maternal nursing. Wetnursing, the only alternative, was subject to criticism. An ignorant class of women were in absolute control of a delicate situation—the care of infants. The nurses were strictly mercenary and were more concerned with their own happiness than with the welfare of the child. The deaths of too many children could be attributed to the faults of these women. It may be asked, what became of the wetnurse's own child when she undertook to feed another? Frequently it was neglected, abandoned on somebody's doorstep or secretly murdered. The countess was aware of this, and she did well to call attention to it. Her pediatric predecessors had argued against wetnurses in a different manner. They had said, for instance, that the complexion and temperament of a red-headed woman could be transmitted to the child through the breast milk. But this and similar threats were of little avail. The countess was on more logical ground, and the most convincing part of the work comes near the end:

> I have found, by grievous experience, such dissembling in nurses, pretending sufficiency of milk, when indeed, they had too much scarcity; pretending willingness, towardness, wakefulness, when, indeed, they have been most wilful, most froward, and most slothful. . . .
>
> Therefore, be no longer at the trouble, and at the care, to hire others to do your own work; be not so unnatural as to thrust away your own children; be not so hardy as to venture a tender babe to a less tender heart; be not accessory to that disorder of causing a poorer woman to banish her own infant, for the entertaining of a richer woman's child, as it were, bidding her to unlove her own to love yours. We have followed Eve in transgression, let us follow her in obedience. When God laid the sorrows of conception, of breeding, of bringing forth, and of bringing up her children upon her, and so upon us in her loins, did she reply any word against it? Not a word; . . .

SUMMARY

A small neglected work, important because it is very likely the second original work in English on a pediatric subject, has been presented. In the words of a better qualified critic, it has been described as "a well wrote piece, full of fine arguments, and capable of convincing anyone, that is capable of conviction, of the necessity and advantages of mothers nursing their own children."

THE "CONDITIONED REFLEX" IN RELATION TO FUNCTIONAL DISORDERS IN CHILDREN*

MAX SEHAM, M.D.
MINNEAPOLIS

An intellectual battle has been waged for almost three hundred years about the psychophysiologic phenomenon known as the "reflex." The chief contestants have been and still are the physiologists and the psychologists, with the anthropologists, the biologists and the physicians allying themselves first with one side and then with the other. It seems that the psychologists were the first to capture the term "reflex"—but of late the physiologists have successfully invaded their territory.

It was Descartes, the great philosopher, who first speculated about reflex activity in the first part of the seventeenth century. He wrote:

> An external or internal stimulus falls on some one or other nervous receptor and gives rise to a nervous impulse; this nervous impulse is transmitted along nerve fibres to the central nervous system and here on account of existing nervous connections it gives rise to a fresh impulse which passes along outgoing nerve fibres to the inactive organ where it excites a special activity of the cellular structures (ref. 41, p. 7; ref. 42, pp. 52 and 380).

Next came the epoch-making treatise on "Reflexes of the Brain," published by I. M. Sechenov in 1863.

Perhaps the most outstanding work on the spinal reflexes was done in the latter part of the nineteenth century and the early part of the twentieth by the physiologist, Sherrington (ref. 44 and 45). In more recent years mention must be made of Thorndike's attempt to apply the known data to a study of intelligence in the field of psychology.[47] And finally there are the brilliant and convincing investigations of conditioned reflexes carried on by Pavlov, the great Russian physiologist, and his disciples during the last thirty years.

The purpose of this paper is to define the terms used, to discuss the nature and the mechanism of the phenomena on the basis of the experimental data at hand, to describe in some detail the experiments of Pavlov and his co-workers, and lastly, to attempt to interpret all of the aforementioned facts in terms of the diagnosis and treatment of functional disturbances in children.

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* From the Department of Pediatrics, University of Minnesota, with the help of a grant from the Graduate School of the University of Minnesota.

DEFINITION OF THE TERMS USED

Since Pavlov was the pioneer and chief advocate of the "conditioned reflex" concept, I shall use his investigations as the chief source of reference and quote him freely. His idea of the "conditioned reflex" is based on the principle that:

> If two stimuli, one of which is the definite stimulus to any reflex action and the other any indifferent stimulus to this reaction, are administered jointly and many times under the same conditions, the latter (the indifferent or negative stimulus) will eventually be grafted on to the ordinary positive stimulus which produces the usual reflex act, i. e., the indifferent stimulus will gradually become the stimulus to a reflex action, even when the usual stimulus to this reflex is not present (ref. 41, p. 26).

For instance, if a dog is given a piece of meat there is almost immediately a natural flow of saliva. This stimulation of the salivary gland by food within the mouth is known as the unconditioned reflex. A bell is now rung every time the meat is given. If this is repeated several times under the same circumstances, the ringing of the bell without the presentation of the meat will bring on the flow of saliva. One is now dealing with a "conditioned reflex." A conditioned response of this kind is therefore caused by the association of an indifferent stimulus (which has been substituted) for one that is biologically adequate to produce the same result, such as the ringing of a bell, the flashing of a light, the scratching of the skin, the sound of a metronome, or the effect of various odors. The development of a conditioned reflex depends on the excitation of some definite point in the cortex, coincidentally with a more intense excitation of some other point, probably also of the cortex, which allows a connection to be formed between the two points; and, reversely, if such a coincident stimulation of these points is omitted for some time, the path becomes obliterated and the connection disrupted. But once such a path has been firmly established it may remain intact without further practice for months and even years. For the formation of a conditioned reflex there must first be an external factor, for example, any stimulus that acts on the analyzer. This in turn produces an effect on some other organ of the body. This association is brought about by repeatedly combining that external stimulus with a physiologic stimulus specific for that particular gland. When the connection is formed, the stimulus that previously had no relation to the gland now affects it as a specific stimulus.

There are certain definite conditions that have to be observed in order to produce the specific responses. First of all, there is the time element. If the intake of food by the animal takes place at exactly the same time with the artificial stimulus, a conditioned reflex will be repeatedly and constantly produced. If a bell is rung for a short

interval first, and the feeding is delayed for two minutes, the salivation will start two minutes after the bell was first rung (without the meat). The time between the application of the first stimulus (the ringing of the bell) and the first flow of saliva is known as the latent period. Such a conditioned reflex is known as a delayed conditioned reflex. If, on the other hand, the food is given first, and then the metronome is sounded, the conditioned reflex cannot be established at all.

The second factor of importance is the state of the nervous system of the animal at the time of the experiment. For example, if the dog is drowsy at the time of stimulation, it is difficult and sometimes even impossible to produce a conditioned reflex. Moreover, the dog must be free from irritations of foreign stimuli that may distract him or give him pain and discomfort.

A third factor is the health of the animal. In order to insure a facility for the establishment of new conditioned reflexes, the animal

Experiment of Nov. 15, 1924

Time	Conditioned Stimulus	Secretion of Saliva in Drops
1:49 p. m.	Sound of metronome	13.5
1:57 p. m.	Buzzer	16.5
2:07 p. m.	Black square	2.5
2 hrs., 7 min., 10 sec., p. m.	(Interval 15 sec.)	3.0
2 hrs., 7 min., 25 sec., p. m.	Sound of metronome	12.0
2:20 p. m.	Buzzer	13.5
2:27 p. m.	Sound of metronome	9.5

The metronome and the buzzer were continued during 30 seconds in each case.

must be in normal health. Fever, infections of any kind and malnutrition will interfere with the certainty of results. A fourth factor is concerned with the properties or characteristics of the stimuli themselves. Powerful and unusually strong stimuli will render conditioning difficult and at times even impossible (ref. 4, pp. 27 and 29).

After a reflex has been established through a specific stimulus, for instance, through the metronome, it is possible to establish a second reflex through the use of another stimulus. This is known as a secondary conditioned reflex. Pavlov wrote:

> A dog has two primary alimentary conditioned stimuli established, one to the sound of a metronome and the other to the buzzing of an electric bell. The appearance of a black square in the dog's line of vision is now used as a further stimulus, which is to be given the character of a secondary conditioned stimulus. The black square is held in front of a dog for ten seconds, and after an interval of fifteen seconds, the metronome is sounded for thirty seconds. In the table for the experiment of Nov. 15, 1924, the square is presented for the tenth time.
>
> Prior to these experiments the appearance of the black square had no effect at all. As seen from the above table, the conditioned reflex of the second order is measured even at this early stage of its development by 5½ drops (2½ plus 3) of saliva during twenty-five seconds (ref. 41, p. 34; ref. 42, p. 105).

INHIBITION

The phase of reflex activity that has been discussed is known as the positive or excitatory, but there occurs an associated process equally important, which is known as the negative or inhibitory phase. The finer differentiations and the complex manifestations of all conditioned reflex activity depend equally on this inhibitory mechanism.

Weber, in 1846, was the first to call attention to the function of inhibition when he discovered the vagus nerve and showed its inhibiting effect on the heart.[18] Shortly afterward, Pflüger isolated the nerves that control the inhibition in the intestines.[18] At the present time experimental evidence seems to point to the belief that inhibitory nerves exist in all rhythmic muscles, in the muscles of the abdominal and pelvic viscera, in the blood vessels, in the muscles of the eye and possibly also in the glandular tissues. Of more recent date, Gaskell and Langley have isolated both sets of nerves in the vegetative system.[18] No good evidence, however, has been furnished to show that the skeletal muscles of vertebrates possess inhibitory nerves, only excitatory nerves having been found in the muscles themselves.

Prior to Sherrington's work inhibition was thought to be merely a negative phase of excitation, that is, merely an absence of excitation. In his epoch-making researches, he corroborated the work of Jackson, who in 1884 observed that hemorrhage in the human brain released from inhibition the spinal center, the activity of which, now unrestrained, produces spasticity. He then demonstrated in monkeys an inhibitory effect on the muscles of the eye, as well as on the extensor muscles of the elbow and knee. He further disclosed that inhibition is a positive function that is of equal importance to excitation. He referred to it as an associate and a counterpart of excitation. Both undergo fatigue, and both have about the same latent periods.[44]

The term inhibition is used differently by various writers, and its connotation depends very much on the point of view of the sponsor. The practicing physician is accustomed to use it chiefly in a negative sense as the opposite of neuromuscular control. He talks loosely and vaguely about the child's poorly developed inhibitory mechanism, having in mind the hyperactive, restless, malpoised child. Many of the nervous disorders in patients he is called on to treat in his daily practice he considers to be the result of unknown abnormal changes in the function of the inhibitory system. The biochemist refers to inhibition as the presence of alkali in the stomach, which inhibits the activity of the pepsin of the gastric juice. The psychologist, in using the term, usually has in mind the cessation or the retardation of a mental function. A stimulus either from within or from without the organism that causes a diminution or a cessation of an act or thought is referred to as inhibition.

It is what Freud called "resistance," and Watson "habit distortion." The attitude of the earlier psychologists toward this phenomenon is best expressed by William James. He wrote:

> Any mental process once begun would continue to the point of exhaustion if not inhibited by other processes. This inhibition is to be explained upon psychical grounds, and consists in a drainage of the sensory impulses away from the active centres corresponding to the mental processes. This drainage brings about a lessened or suspended activity of that special process. One mental process can then inhibit another by appropriating its nervous energy. On the other hand, interference of any mental process by irrelevant sensory stimuli pressing in upon its centres, may be inhibited by a drainage of those sensory currents downward into some other path which is kept open by muscular activity such as twirling a pencil or fumbling with a watch chain during deep thought. Thus inhibition is an essential element in cerebral life which on the one hand makes possible the entrance on the stage of consciousness of only one set of sensations at a time and so preventing a hopeless jumble and on the other hand provides for the arrest of any mental activity when it has served its purpose.[22]

Howell, the physiologist, defined inhibition "as a suspension of functional activity." [18] He said that it is as important as excitation in the adjustment of the organism to its environment. The physiologist Bayliss wrote, "inhibition is any process which stops action in progress by application of some influence from without."[18]

Since 1845, many theories have been proposed to explain the nature of the inhibitory process. In some an attempt has been made to find a fundamental principle that would explain inhibition wherever it occurs in the body. Other theories are limited to an explanation of this process as it occurs in the central nervous system. Some writers believe that the physiology of inhibition may be different in different tissues, i. e., different in the central nervous system from that in the cardiac tissues.

In summing up the entire subject chiefly from a physiologic point of view, it is well to quote from Howell in his review of the subject (ref. 18, p. 168).

> 1. Inhibition is fundamentally the same process in all tissues and it is probable that a general theory of inhibition may be formulated to cover all cases.
>
> 2. Inhibition is produced in all cases through specific inhibitory nerves. The evidence for this proposition is quite strong as regards the inhibition of the heart, the blood vessels, the plain muscles of the pelvic abdominal viscera and the glands.
>
> 3. As regards the nature of the inhibitory process there is almost no scientific information. One point upon which there seems to be sufficient ground for agreement is, that the physiological mechanism of inhibition which is exerted through the agency of the nervous system is probably similar throughout and acts upon the chemical system in the cells. This process may be affected not only through nerve impulses but by chemical messengers, or hormones.

There are seven chief theories regarding the locus and nature of the inhibitory process which deserve consideration either because of the historical interest or of the experimental evidence offered. First Setsche-

now and Langendorf claim that there is a specific inhibitory nerve center in the brain. They claim to have found it in the optic nerves. Second, the so-called "interference theory" was proposed by von Cyon in 1870, who thought that two nerve impulses following simultaneously into a nerve cell might be obliterated just as light or sound waves might interfere with one another. This opinion, however, was abandoned by von Cyon himself in the face of further evidence. In its place came the newer "decreement," "impairment" or "interference" theory of Lucas, modified and adopted by Adrian. In short, it is as follows:

> Central nervous paths are conceived as possessing properties similar to those observed in isolated nerves. Since it has been found that when nerve trunks are stimulated above a certain critical frequency, conduction ceases across regions of subnormal conduction (e. g., the neuro-myal junction). It has been assumed that similar "interference" occurs along central nervous pathways and under appropriate circumstances that this leads to cessation of activity (e. g., to central inhibition).

The third theory, proposed by Gaskell in 1884, is based on the inhibitory action of the cardiac muscle (anabolism theory). He suggested that inhibition represented the anabolic phase of metabolism. This idea was severely criticized by MacDougall, who, in 1903, proposed the drainage hypothesis instead. He suggested that the transmission of energy along the nerve fiber is to be compared to the flow of liquid through a conduit, using a simple function of physics ("if water is flowing through a series of pipes under a given head of pressure, and the resistance is lowered through one of the pipes, more liquid will flow along that path and less along the others"). In the same way, the flow of energy becomes inhibited in these latter paths. Using this analogy, he proposed that a nerve, if stimulated, becomes a path of low resistance and deflects to itself some part of the energy that was flowing along other fibers and which, consequently, show the phenomena of inhibition. His theory has not been substantiated by experimental evidence. The fifth and sixth theories regarding the nature of inhibition are those of Sherrington and Verworn, both physiologists, based chiefly on experimental and objective studies on animals. The former believes that the locus of inhibition lies in the membrane at the synapsis or the myoneural junction. The latter says that inhibition is brought into play as the refractory state that follows an impulse in an excitable tissue. He postulated the idea that there is a liberation within or about the perikaryon of nerve cells of a specific inhibitory substance that antagonizes a similar specific excitatory substance produced at the same region (ref. 18, pp. 167-170). Pavlov (seventh theory) assumed that inhibition spreads like excitation from its point of origin over wide areas of the cortex, and that the inhibitory impulses are transmitted from point to point. According to others, this theory may be true as regards central inhibition,

but they say that there is not sufficient evidence of the conduction of the inhibitory state in any of the peripheral tissues in which inhibition is known to occur. Although some of Pavlov's conclusions are disputed by eminent physiologists, he has brought to attention many important facts on the subject. He has shown the various influences of various stimuli on inhibition under various circumstances, and he has given a working as well as a scientific classification of the different forms of inhibition. He believes that the inhibitory process arises in the nerve cells themselves and not in the connecting path between those cells; that the mechanism of development of a conditioned reflex and the mechanism of external inhibition are somehow similar, and that the process of external inhibition bears some relation to the development of new connections between different cortical elements.

He recognizes two kinds of central inhibition, external or indirect and internal or direct. The former he defines as "the activity of one centre brought about as the result of the activity of another centre which has arisen as the result of excitation from some afferent nerve" (ref. 41, pp. 43, 46 and 68; ref. 42, pp. 125 and 134). An example of external inhibition is the inhibition of the heart beat by the stimulation of the vagus. This is an inherited or unconditioned phenomenon. This form of inhibition is brought about as follows: The dog and the experimenter would be in the midst of an experiment with the usual conditions obtaining, and then suddenly something unusual would happen, such as a loud noise from without. If this extraneous noise occurred at the time of the application of the conditioned stimulus, it would usually cause either a decrease or a disappearance of the reflex response.

What is meant by internal inhibition is well shown by an experiment conducted by Pavlov. If a conditioned reflex is established in a dog by substituting a skin stimulus for that of the food, one can in the beginning obtain it from contiguous regions of the skin, as well as from the original point of stimulation. If, however, at the same time that the food is given only this one point is stimulated, and the food is not given when the other points are stimulated, then one can localize the conditioned reflex to only one point. The food reflexes from the other points will gradually disappear, owing to what Pavlov calls "internal inhibition" (ref. 41, p. 43; ref. 42, 125). This form is acquired or conditioned. He has divided this process into the following four groups:

1. If the conditioned stimulus is not reinforced by association of the unconditioned stimulus after a number of repetitions, the conditioned stimulus that has been developed will become extinct. This is known as extinction inhibition (ref. 41, p. 49; ref. 42, pp. 134 and 139).
2. There is the delayed reflex, which has already been mentioned,

referred to by Pavlov as the memory reflex. 3. This is a more complicated form known as conditioned inhibition (ref. 41, p. 68; ref. 42, pp. 125 and 160). Suppose that a positive conditioned stimulus has been established in a dog by the usual means of meat and a bell; then a new stimulus in the form of a different kind of a sound as, for example, that of a metronome is added. If the two stimuli are applied at the same time no flow of saliva results. In other words, when this new stimulus (metronome) is added at the same time as the conditioned stimulus the combination does not evoke the conditioned reflex. If, on the other hand, the first stimulus is applied alone and with constant reinforcement, it will have its positive influence. Pavlov called this phenomenon conditioned inhibition, and the additional stimulus the conditioned inhibitor. 4. He described the inhibition of differentiation in the following way, "A mechanical stimulation of a definite area of the skin is used as a conditioned stimulus" (ref. 41, p. 117; ref. 42, pp. 238 and 299). The same tactile stimuli are then applied to other parts of the skin getting nearer and nearer to the first area stimulated. The stimulation of these other parts produces the same effect; namely, they act as conditioned stimuli. If, however, the stimulation of these parts of the skin is repeated with an accompaniment of feeding and while other parts of the skin are stimulated without giving food, the stimulation of the latter parts gradually loses its effect as a positive stimulus.

In summing up Pavlov's ideas on inhibition, I can do no better than to quote him again. On this subject he wrote:

> The physiological mechanism of the effect of these stimuli is as yet obscure, neither do I find it possible to discuss the problem of inhibition in its entire range. The experimental material, although considerable, is not yet sufficient to establish any general and definite conception of the nature of inhibition and its relation to excitation. Explanations which seem to fit some one group of phenomena fail when applied to other groups. Many observations do not fit in with any of the theories, and our conception of the mechanism involved has had to be changed many times in the course of our research, never entirely satisfactorily. Here again, as in the whole of our research, we can only collect and systematize facts. We change, for example, the manner in which the conditioned stimulus is reinforced by food. Instead of a plate automatically moving with food from behind a screen a measured amount of food is now delivered mechanically into a stationary plate. Many dogs after this change persistently decline the food, and all conditioned reflexes disappear. This, of course, is a case of inhibition, but what explanation can be suggested as to its mechanism? It may be compared with an observation discussed previously where a change in the sequence of a series of conditioned stimuli led in some animals to a more or less profound inhibition of the entire conditioned activity—an inhibition which lasted for several days, notwithstanding that a return was made to the previous order, to stimulation. What happens here with a small number of conditioned stimuli can well be imagined to take place in respect to the entire environment. Constant repetitions of external events in a stereotyped order may lead to a definite stereotyped pattern of activity in the cortex, each new distribution of the stimuli now producing a disturbance in

the pattern of the cortical activity, leading to inhibition in exactly the same manner as in our experiments with alteration in the sequence of the conditioned stimuli. This comparison does not, however, explain the mechanism of the development of inhibition in this particular case. Was it a result of the investigatory reflex due to the change in environment, or are the investigatory reflex and this very prolonged inhibition two independent phenomena? In favor of the first supposition the fact can be advanced that in very inhibitable dogs the investigatory reflex exercises an extraordinarily prolonged inhibitory after-effect (ref. 41, pp. 395 and 396).

THE PHYSIOLOGIC BASES OF FUNCTIONAL DISTURBANCES

The important question, of course, that all this leads up to is whether the data collected and the conclusions arrived at by Pavlov, Krasnogorski and his co-workers can be applied to human beings. I have discussed so far the nature and mechanism of conditioned reflexes and have shown in detail several of Pavlov's experiments. The significance of the data obtained as applied to man can best be understood in Pavlov's own words. He said:

> In applying to man the results of investigation of the functions of the heart, digestive tract and other organs in the higher animals, allied as these organs are to the human in structure, great reserve must be exercised and the validity of comparisons must be verified at every step. Obviously, even greater caution must be used in attempting similarly to apply our recently acquired knowledge concerning the higher nervous activity in the dog—the more so, since the incomparably greater development of the cerebral cortex in man is preeminently that factor which has raised man to his dominant position in the animal world. It would be the height of presumption to regard these first steps in elucidating the physiology of the cortex as solving the intricate problems of the higher psychic activities in man, when in fact in the present stage of our work no detailed application of its results to man is yet permissible.
>
> Nevertheless, inasmuch as the higher nervous activity exhibited by the cortex rests, undoubtedly, on the same foundation in man as in the higher animals, some very general and tentative inferences can even now be drawn from the latter to the former.
>
> In the future it may confidently be expected that a full and detailed knowledge of at least the elementary facts of this activity will be obtained as regards both normal and pathological states. The similarities between the manifestations of this activity in man and animal being more obvious under normal conditions, I shall dismiss these briefly, discussing in more detail certain pathological cases.
>
> It is obvious that the different kinds of habits based on training, education and discipline of any sort are nothing but a long chain of conditioned reflexes. We all know how associations, once established and acquired between definite stimuli and our responses, are persistently and, so to speak, automatically reproduced, sometimes even although we fight against them. For instance, in the case of games and various acts of skill, it is as difficult to abolish all sorts of superfluous movements as to acquire the necessary movements; and it is equally difficult to overcome established negative reflexes, i. e., inhibitions. Again, experience has taught us that difficult tasks should be approached by gradual stages. We know also how different extra stimuli inhibit and discoordinate a well-established routine of activity, and how a change in a preestablished order dislocates and renders difficult our move-

ments, activities and the whole routine of life. Again, we know how weak and monotonous stimuli render us languid and drowsy, and very often lead to sleep. We are also well acquainted with different cases of partial alertness in the case of normal sleep, for example a sleeping mother next to her sick child. All these phenomena are analogous to those constantly met with in our animals as described in the preceding lectures (ref. 41, pp. 395 and 396).

One of the strongest criticisms that has been made against the surgical investigation of the function of the nervous system is that in the experiment the damage that is done to the organ operated on interferes with the accurate interpretation of the results. This objection Pavlov has eliminated in the study of a large number of dogs, in which functional disorders occurred without having produced any change in the tissues or organs. While subjecting the dogs to these various forms of stimulation, he noticed that under certain circumstances certain dogs reacted in unusual and unexpected ways, which for a long time he was unable to explain. These disorders were purely of a functional origin and not due to surgical intervention or trauma. The observations he made may also have a great therapeutic value because the animals recovered spontaneously by the mere removal of these stimuli; in other words, by stopping the experiment. In other instances the disturbances were so persistent as to require drug therapy. An outstanding observation was the individual variation in behavior reaction of different dogs to the same stimulation and presumably carried out under exactly the same controlled condition. In some dogs the conditioning would produce severe and prolonged disturbances; in others the same influences would create only mild and transient effects, and still others no effect at all. On the basis of the reactions of these dogs to stimulation and conditioning, he tried to classify their nervous systems. One type was what might be called hyperkinetic; they were restless, continuously on the go, alert and keen and very quick to react to the faintest stimuli. These animals, when placed in the stand and limited in their movements, became drowsy very quickly and were easily inhibited, their conditioned reflexes diminishing or even disappearing. However, if many stimuli were used and many conditioned reflexes were developed at the same time, these dogs became quite satisfactory subjects for the experiments. In other words, if they were exposed to quick changes of varied stimuli, they were quite energetic, but with the slightest monotony in stimulation they became dull, drowsy and inactive (ref. 41, p. 285). The second type of dog represents the other extreme. These animals are extremely shy and restrained. At the slightest movement or noise they show great fear. They get used to their experimental environment very slowly. If the experimental conditions remain the same, their conditioned reflexes remain extremely stable and regular (ref. 41, p. 287). The first type has been called the excitatory, and the second, the inhibitory.

Of course, all dogs do not belong to either one or the other type; there are many intermediate types. Those that have a predominance of excitatory processes are rather lively and active, and those that approximate the inhibitory form are quiet and restrained.

Whether or not Pavlov is right in believing that the temperament of dogs is entirely inherent cannot be discussed at this time. Furthermore, it remains to be proved that this analogous difference in children depends only on hereditary influences and not, as the behaviorists would have one believe, on the acquired habits of training and education. It is impossible to describe all of the functional disturbances that were produced experimentally or observed accidentally by Pavlov and his co-workers. However, one or two examples might be of interest. For example, in one dog a conditioned alimentary reflex was developed to an electrical stimulation of the skin. Ordinarily, if an electrical stimulus is applied to the skin of a dog, he responds by drawing away, but if weak currents are started at the same time the dog is fed, the defense reaction can soon be overcome, and this stimulus can be used as a substitute for the natural food reflex. In this way the conditioned alimentary reflex was established and remained stable for many months. The animal remained perfectly normal throughout a long period of time, but after a certain time this conditioned stimulus began to have negative results. Salivary secretion became more and more delayed. The attempt was made to apply the electrical stimulus to other places than the one for which the reflex had been originally developed. Soon everything changed abruptly. Instead of any salivary secretion representing a positive response, the animal reacted with a violently abnormal behavior, his extreme excitement reaching the point of mania. This happened to two other dogs under similar circumstances. In none of these three dogs could anything be done to restore at once the alimentary reflex to the electrical stimulus. In one dog it was necessary to stop the experiment for three months before the original alimentary conditioned reflex would return. In all dogs the experiment resulted in a chronic functional disturbance of the nervous system (ref. 41, p. 289). Pavlov believes that this disturbance is due to a clashing of excitation with inhibtion, which resulted in a disturbance of the balance of these two phenomena.

One more example will be cited to show the significance of these facts. An excitable type of dog was conditioned to the metronome, the buzzer, a bubbling sound and tactile stimulation of the thigh (ref. 41, p. 296). At the same time negative reflexes were created by the combination of a hissing sound with the metronome and a tactile stimulation of the shoulder. All of the positive conditional reflexes were delayed for three minutes. When the former were applied, salivary secretion resulted; when the latter, there was an absence of salivary secretion. From March until August these reflexes were constant. In

August, the electric current was considerably increased in strength, and a definite change resulted. The delayed reflexes became disturbed, and conditioned inhibition became incomplete. Things were done to secure the previous reactions of the animal, but to no avail. The animal lost weight and became very dull. He was then given complete rest for a considerable time. A larger amount of food and cod liver oil was administered. It took a considerable time before the experimenters were able to establish positive alimentary conditioned responses. Although in these two dogs the irritating influences were identical, they reacted in opposite ways. In the excitable dog the inhibitory function became weaker, and in the quiet dog the excitation became weaker. It was only after the administration of bromides to the excitable dog (100 cc. of a 2 per cent solution of potassium bromide daily in the form of an enema) that the animal became normal in his responses. The bromides were administered for eleven days, and the cure was permanent, the conditioned reflexes remaining normal for the remaining two and one-half months of the experiment. Bromides did not help the other dog. He was left alone for a very long time, and he recovered spontaneously and completely. In all the other experiments, and there were many of them, the same causal explanation is given.

Another contribution to the pathogenesis of functional disturbances was made as a result of an incident that happened in 1924. During the big flood that occurred in Leningrad, Pavlov observed that his dogs showed prolonged nervous disturbances. The animals had to be transferred during the storm from their usual quarters by making them swim from their kennels into the laboratory. All of the animals remained quiet and huddled up. Some of the dogs continued in their usual responses. Others, on the other hand, became so inhibited that nothing could be done with them. The strong and extraordinary stimuli that produced an acute "neurosis or psychosis" in these dogs during the flood are comparable, according to Pavlov, to the influence of such stimuli as grief and excitement in man, which often lead, when the natural reactions are inhibited by the necessary restraint, to profound and prolonged loss of balance in nervous and psychic activity. So, too, neurosis and psychosis may develop as a result of different powerful stimuli, e. g., extreme danger to oneself or to friends, or even the spectacle of a frightful event not affecting one directly. The same influence may produce a profound disturbance in one person and show no trace of effect on others, according to the power of resistance of the nervous system in each case. Dogs, like human beings, show a great variation in the ease of production of functional disturbances. One of the most efficacious methods of evoking nervous disturbances in dogs, namely, a direct transition from an inhibitory to an excitatory

rate of stimulation of the same area of the skin, failed to produce the slightest effect after a great number of repetitions on many dogs. In other dogs disturbance occurred eventually after many repetitions, while in some it was possible to create such disorders in a few attempts (ref. 41, pp. 289 and 396; ref. 42, pp. 348 and 364).

THE CONDITIONED REFLEX IN THE CHILD

While Pavlov has concerned himself with experimental investigations in animals, Krasnogorski has studied this subject in children for twenty years. His first experiment was with a 14 months old baby.[25] He used the salivary gland as the organ for conditioning. He "excited" the infant by presenting milk in a glass without giving the milk, and observed the frequency of swallowing movements. With the flow of saliva increasing, swallowing resulted, and he judged the amount of flow by the number of swallows in a given time. Later he took into

Record of Number of Swallows in Three Minutes

	First Observation	Second Observation	Third Observation
Before stimulation	1	3	3
	3	3	2
	0	2	3
	2	1	3
Excited by food	9	16	10

account not only the salivary secretion as represented by the number of swallows, but also any movements of the mouth that took part in the process of eating. He recorded all these movements by a kymograph. In this way he measured objectively the latent time and the height and durability of the curve.

He then used an auditory stimulus by means of ringing a bell. The following results were obtained in a three to five minute interval after the ringing of the bell:

Record of Number of Swallows in Three to Five Minutes

	First Observation	Second Observation	Third Observation
Before excitation	3	3	5
	4		
	2	3	4
	2		
	0	2	4
During stimulation	6	8	8

Krasnogorski next started three children, one 3 and two 6 years old, respectively.[24] He established the conditioned reflex in the first one by ringing an electric bell for one minute and feeding one-half teaspoonful of honey every third minute, fifteen seconds after he had started

the ringing of the bell. The experiment was repeated until the ringing of the bell in itself caused the feeding movements. In the 6 year old children he developed the reflex by sounding a tone on a reed pipe, chocolate being given ten minutes after the first sound of the reed. He also used cutaneous stimulation, scratching the skin with a camel's hair brush for one minute, and feeding chocolate fifteen seconds after the irritation. He studied the effect of other stimuli and the permanence of these reflexes. In 1913, he presented a short summary of his work before the International Medical Congress, in which he asserted that stimuli of sight, of hearing and of the skin can be changed into specific stimuli, and that, when applied under certain circumstances, they will create specific motor responses.[30] In the same year,[25] he reported his findings on pathologic children, in whom he had studied the more complicated functions of conditioned inhibition and inhibition of differentiation. He claims to have been able to establish conditioned reflexes in all normal children beyond the age of 1 year, in from two to ten trials. His procedure was as follows:

EXPERIMENT 1.—A child, aged 6, was conditioned to the metronome. When the reflex was stabilized, the child was able to differentiate 92 from 144 beats. The latter was used as the positive stimulus, being accompanied by feeding. The former was the negative stimulus. The latter was constantly accompanied by feeding and occasioned the conditioned reflex; the former was inactive because the child never received food with it. The differentiation was formed as early as the sixth repetition of the experiment. Krasnogorski wrote: "We made differentiations which were more difficult, that is, between 144 and 108 beats of the metronome. This differentiation was also quickly accomplished by the child by means of five nonsupported irritations (104 beats). Then followed the experiment of bringing the active and inactive stimulators still nearer to each other, that is, 144 and 120 beats were applied. This differentiation was formed after four nonsupported irritations, but the conditioned reflex activity of the child had changed. The latent periods of conditioned reflexes had increased in length twice (instead of 0.4 to 0.5 second it became 0.8 to 1.9 seconds; experiments performed on May 29 and 31). At the same time we observed an important change in the behaviour of the child; having always been easy to deal with and quiet during the experiments, he now became irritable and refused to go to the laboratory. Once more we made a differentiation which was still more difficult, that is, between 144 and 132. During the work which now began, we were informed from the child's ward that the patient had become nervous: he had always been well behaved; now he cried often, beat the other children and said he wanted to leave the hospital. The experiments had to be discontinued, as not only no differentiations could be formed, but even the differentiation of June 18 between 120 and 144 beats of the metronome had disappeared (experiment performed on June 18). The inactive stimulation of 134 beats began to cause yawning and sleepiness, and during the fourth stimulation the child went to sleep, which happened for the first time in the course of the whole work of five months" (experiment performed June 22, table 1).[29]

EXPERIMENT 2.—"S. G., a girl, aged 12, was taken to the Children's Clinic of the Medical Institute with symptoms of globus hystericus and frequent vomiting after the ingestion of food." A year before, the patient had drunk some anisated

solution of ammonia by mistake, and after this she began to vomit. She was brought to the hospital, where, however, the physicians did not find any symptoms of poisoning. From that time the patient continued to vomit after eating, when excited. When the patient was excited (stimulated) on an empty stomach, dyspnea, cyanosis and twitching of the muscles of the face occurred, instead of vomiting. Thus, the stimulation had two different effects: with a full stomach, it radiated to

TABLE 1.—*Findings for Four Months*

Date	Number of Stimulations	Time	Stimulation	Conditioned Reflex	Latent Period, Seconds
3/6	91	12:04	Metronome 144	×	0.4
	92	12:07	Metronome 144	×	0.5
	93	12:13	Metronome 144	×	0.4
	94	12:15	Metronome 144	×	0.5
4/4	159	3:05	Metronome 144	×	1.2
	10	3:07	Metronome 92	0	—
	160	3:09	Metronome 144	×	1.5
	161	3:11	Metronome 144	×	1.0
	11	3:14	Metronome 92	0	—
	162	3:17	Metronome 144	×	1.3
5/21	267	1:09	Metronome 144	×	0.9
	268	1:12	Metronome 144	×	0.9
	6	1:15	Metronome 108	0	—
	269	1:18	Metronome 144	×	...
5/29	275	2:48	Metronome 144	×	1.2
	7	2:51	Metronome 108	0	—
	276	2:54	Metronome 144	×	0.7
	277	2:57	Metronome 144	×	0.7
	1	3:00	Metronome 120	×	2.0
	278	3:03	Metronome 144	×	0.6
5/31	280	2:01	Metronome 144	×	0.8
	281	2:04	Metronome 144	×	0.9
	282	2:07	Metronome 144	×	0.8
	283	2:12	Metronome 144	×	1.0
6/8	321	12:38	Metronome 144	×	1.2
	322	12:41	Metronome 144	×	0.7
	4	12:44	Metronome 120	0	—
	323	12:47	Metronome 144	×	1.0
	324	12:50	Metronome 144	×	1.5
	1	12:53	Metronome 132	×	1.7
	325	12:56	Metronome 144	×	0.9
6/81	330	12:40	Metronome 144	×	1.2
	6	12:43	Metronome 120	×	5.3
	331	12:47	Metronome 144	×	2.0
	2	12:50	Metronome 132	×	3.0
	3	12:53	Metronome 132	×	2.0
	332	12:56	Metronome 144	×	0.9
6/22	348	1:04	Metronome 144	×	...
	12	1:07	Metronome 132	×	1.1
	13	1:10	Metronome 132	×	0.5
	14	1:15	Metronome 132	×	1.4
	349	1:25	Metronome 144	×	0.8

the vomiting center, and with an empty stomach, to the respiratory and circulatory centers.

"When our patient was first brought to the laboratory, she exhibited an intensive passive-defensive reaction. Usually there is no difficulty in putting the children on the table for experiments, but in this case another child had to be called and placed in the apparatus, before she would lie down.

"Then in five minutes we stimulated her by the beats of the metronome. This stimulation produced intensive excitement, which was expressed by dyspnea, cyanosis and convulsions of the muscles of the face. The second stimulation had the same result. The third stimulation caused a weaker reaction, and, beginning with

the fourth, one new fact was observed. The metronome from the first beats began to cause intense sleepiness in the child. As soon as the metronome began to act, the patient closed her eyes, breathed heavily and held a biscuit between her teeth during the whole time of the action of the metronome. One or two minutes after the stimulation with the metronome, the sleepiness passed, and she began to eat the biscuit. Thus the metronome, which at first developed intensive stimulation, now caused inhibition. Two or three seconds after the beginning of its action the child was dazed by a strong, stable, widely radiating inhibition (experiment performed on January 18, table 2).

"Then, together with Professor Pavlov, we decided to make this inhibition conflict with intense excitement. We made the following experiment: we wanted to see what would happen if we applied the metronome, not when the child was having full rest, and the innumerable impulses from muscles, ligaments, and articulations were minimal, but in conditions of extreme motor excitement, that is, in dancing. That was easy enough, as the patient thought that she could dance well.

"For once, we broke our rule of not entering into any conversation with the patient, and in this special case asked her to dance. She began to do so, and when she reached the greatest motor effect, the metronome was put in action. The patient stopped instantly; for a minute or so she stood bending her body slightly to and fro with her eyes fixed on one point; then dyspnea, tremor and cyanosis developed quickly and she began to sob. When in ten minutes, it was possible to put her back into her place, she ceased crying, lay quietly, but refused to take a biscuit. The experiment was interrupted (experiment performed on January 24, table 2).

"On the second day, the patient refused to go to the laboratory. The following day, she went, but, as before, showed a strong defensive reaction to the surroundings. However, she lay down in her place and was more or less quiet. As soon as the metronome was set in action, she stopped her ears, her respiration became quicker, her face reddened, and the muscles of her feet twitched. When the metronome ceased she was quiet again. The same thing was observed every time the metronome was started. During the next two days the metronome produced the same effect. On the third day, the reaction of excitement from the metronome gradually began to be less; it did not disappear until the sixtieth day. But now the metronome had lost its inhibitory power, which it developed so intensively before our experiment with the dance. Our patient did not sleep now, neither did she appear to become excited. We were able to form the conditioned reflex with this stimulator. The reflex was being formed extremely slowly. Only at the one hundred and forty-fifth trial did a slight reflex appear; for a long time it was very unstable, and only at the two hundred and ninety-fifth trial did it become constant. It is interesting that the further study of this reflex showed that it disappeared very slowly; about ten stimulations unaccompanied by food were necessary to cause the conditioned reflex to disappear. The reflex which was formed with extreme difficulty, was also with difficulty inhibited.

"From these experiments we see the difference between the reaction produced by external stimulation in a normal and in a pathologic child. The whole activity of the cerebral hemispheres in a normal child is founded on a flexible balance between the excitatory and inhibitory processes; here excitation and inhibition regularly and easily replace one another, depending on changing external circumstances. In our pathologic case this flexibility of the balance was lost. We could see that the metronome at first acted for a long time as an intensive inhibitory agent. After that, it produced extreme excitement for five days. Then for a certain time, the

balance was restored, and we could form the conditioned reflex. However, this reflex could be made to disappear with great difficulty, because now inhibition was lacking. Thus instead of a normal flexibility of the balance, inhibition (sleep) or extreme excitement prevails.

"Our experiments show the consequences when intense excitation conflicts with strong inhibition. An extended and great disturbance of the balance occurs even if such an elementary activity of the cortex as the formation of conditioned reflexes is obstructed. In life such conflicts always take place, but in the normal nervous system a disturbance of balance is quickly restored. However, it acquires a more serious character when several severe conflicts follow one another, or when the child's central nervous system itself shows some pathologic inborn deficiency."

The following is a summary of Krasnogorski's claims: 1. He is able to differentiate, in fact, classify, the nervous make-up of children (whether they are normal, neuropathic or psychasthenic) by the way

TABLE 2.—*Results of Experiments*

Date, 1924	Number of Stimulations	Time	Stimulation	Conditioned Reflex	Feeding
1/18	24	3:05	Metronome 138	Sleep	Feeding
	25	3:09	Metronome 138	Sleep	Feeding
1/24	36	1:10	Metronome 138	Sleep	Feeding
	..	1:16	.....	.....	.....
	..	1:17	.....	.....	.....
	37	1:19	Metronome 138 and dancing	.....	.....
	38	1:29	Metronome 138	.....	Feeding
1/26	39	12:52	Metronome 138	.....	Feeding
	40	12:55	Metronome 138	.....	Feeding
	41	1:01	Metronome 138	.....	Feeding
1/28	42	12:04	Metronome 138	.....	Feeding
	43	12:07	Metronome 138	.....	Feeding

In table 2 the experiments to condition a hysterical child are described.

they respond to efforts at conditioning. 2. He is able to produce conditioned reflexes on all children from the age of 2 years and up. 3. Children who are neurotic or mentally defective are less easy to condition, and the reflexes established in the latter are difficult to maintain and cannot be made permanent as in normal children. 4. A large number of functional disturbances to which children are prone, such as enuresis, tics and insomnia, are the result of unfavorable conditioned stimuli. 5. Many factors influence the activity of conditioned reflexes, as, for example, fever and the health of the child. 6. Fatigue and neurosis can be explained on the basis of a disturbance of balance between excitatory and inhibitory stimuli. 7. The more stable the nervous system, the more easily can new conditioned reflexes be established and the more easily can old reflexes be abolished. 8. He can determine the state of the inhibitory mechanism by the responses of the individual child to the way he "conditions." "Conditioned

inhibition develops in normal children in from five to ten trials, and disappears slowly if left to itself." 10. In pathologic conditions (he does not say specifically in which diseases) "the inhibition develops more slowly, and disappears more quickly." 11. In neuropathic children (his definition is vague) "the inhibition is different in different types." "The excitable neuropath develops inhibition easily, which breaks down easily, and disappears rapidly." "In the phlegmatic child, inhibition develops slowly, and only in response to relatively strong stimuli, and may last a considerable period." 12 He, Krasnogorski, through this method (he does not exactly say how), can predict the outset of a convulsion in an "epileptic" patient. 13. In a recent appraisal of his own work and that of his associates, Krasnogorski, before the International Congress of Pediatrics (1930),[33] made a summary of his most important conclusions. He found that in cretins in whom the establishment of conditioned reflexes is very difficult or entirely impossible, treatment with "thyroidin" increases the excitability of the cortex and augments both conditioned and unconditioned salivary reflexes. To quote him further:

> An ill reflex has a certain pathological influence on adjacent reflexes; a temporary pathological area, as it were, a functional "ulcer," is formed around it. . . . Every touch to this "ulcer" produces a pathological irradiation or inhibition and also pathological induction in the surrounding parts and in this way the pathological focus immediately influences the whole activity of the cerebral hemispheres. There develops a temporary local neurosis. In healthy strong nervous systems these functional nervous disorders are quickly healed, the strong nerve cells quickly restore their optimal excitability and a normal equilibrium between excitability and inhibition. In children with constitutionally defective cortexes the weak cells are unable to restore their normal excitability speedily, and therefore the pathological focuses may remain in the cerebrum for a long time.

I am rather reluctant to criticize the foregoing claims, because I have not had access to all of the Russian references. Moreover, the ambiguous use of such terms as "ulcer," "heal" and "weak" in the discussion of physiologic processes may be explained more fairly on the basis of a lack of command of the English language rather than because of a deficiency in reasoning. The following lines, therefore, will be more in the nature of questions than criticism.

It can be seen in table 1 that from March 6 until May 31 the child was well balanced and made no objection to getting into the apparatus, but on May 31 he refused to go to the experiment, and became rather silent. Why should the introduction of the inhibitory stimuli of a metronome at 108 and 120, as of May 29, be solely responsible for the change of behavior on May 31? Evidently, nothing had been done during the ensuing week, yet the child still suffered from abnormal behavior. On that day, too, the inhibitory stimuli of 120 and 132 were used.

Nothing was done until the eighteenth, at which time the latent period became very much increased, with three negative stimulations, one of 120 and two of 132. Following this event, the child was rude and extremely excited and disobedient.

In table 2, the experimental evidence does not seem to justify the conclusions drawn from the single case. Could the change of behavior not be due to fatigue or to the displeasure of the child at being subjected to unpleasant stimulation? Is the stimulation with a metronome at the rate of 138 specific enough to produce such behavior? Would a metronome of 135 or 140 have done the same thing? Would a repetition of the experiment produce the same results in this child? Is not the behavior of a hysterical child too variable and too easily influenced by many external factors to justify the foregoing conclusion? All the other tables presented by Krasnogorski are subject to similar criticism, namely, an insufficient number of controlled cases and an inadequate consideration of individual differences in normal children. Moreover, in his study of pathologic states, Krasnogorski groups all children together, whether they are idiots, epileptics or psychopaths or even are suffering from organic lesions of the brain, and calls them neuropaths, using one or two examples from each group. One can hardly expect the same cortical responses from an idiot as from an epileptic child or a psychopath, or even from one suffering from an organic lesion of the brain. Nor does Krasnogorski take into consideration the wide range of individual differences in normal children, the differences due to chronological age or the emotional reactions of the child to the experiment and to the experimenter.

Can the concept of conditioned reflexes be made to explain the pathogenesis of common functional disorders in children, such as tics, insomnia, enuresis, certain types of convulsive seizures, neuromuscular restlessness and other such signs and disorders? Its advocates, among them Mateer, Burnham and Watson in America, explain such disorders on the basis of unfavorable conditioned reflexes. They explain neurosis in the same way as they do fatigue; they believe that the same causes are responsible for tics as for insomnia.

Take the case of what is commonly known as school sickness. A child who is late for school rushes through his breakfast, feels extreme anxiety as to the outcome (scolding, humiliation, etc.) and finally speeds off to school. After arriving there, he vomits. On the following day, although there is no rush or anxiety, he vomits again. The behaviorists will associate such vomiting with an unconditioned stimulus, namely, food, yet unless one has specific information as to the time relation between the two, it is extremely difficult to say with certainty that such an explanation is the only valid one. A disorder of this kind might be

explained in other ways, for example: it is known that there is a definite physiologic relation between the emotions (cause) and some functional disturbances (effect). Strong emotions, such as grief or worry, will interfere with digestion, and in certain persons will cause gastric symptoms. School itself may be the emotional irritant sufficient to produce vomiting. Furthermore, it is plausible to suppose that for some time afterward the same irritant (anxiety or worry) may produce the same effect. It appears to me that this explanation is fully as objective and is based on as sound physiologic principles as the other. Another example is blinking of the eyes. A child gets a coal cinder in its eye. The cinder is removed. The natural reaction to such a stimulus is blinking. After several days, frequent blinking develops which may persist after the causative stimulus has been removed. This may occur especially in children with an unstable nervous system, but it may also occur in normal children. If a drug that reduces the pain in the eyelid is given early, the stimulus will be eliminated, and the formation of the unfavorable reflex, namely, the tic, will be prevented. Or take another example. A child, 2 years of age, in a fit of temper, happens to hold its breath while crying. The crying is the stimulus that stops the respiration. Repeated attacks of crying bring on the same reflex, and soon the child becomes a "breath holder." It has always been thought that the cause of this disorder was the hyperirritable adductor muscle of the larynx associated with spasmophilia. The explanation of the pathogenesis of this condition on the grounds of a conditioned reflex seems more logical. And yet in order to explain the establishment and the persistence of such a disorder by means of the "conditioned reflex" theory, it is necessary to have a more definite association between the negative stimulus, such as the coal cinder, and some unconditioned natural stimulus.

TREATMENT

If the conceptions of Pavlov and Krasnogorski and their co-workers are fundamentally sound, treatment for these functional disorders based on this idea should be successful. Pavlov found that rest and interruption of experiments in many cases helped in the restoration to normal conditions. One of his dogs was brought into an extremely excitable state by a clash of the inhibitory with the excitatory processes.

> All forms of inhibition were disturbed, all negative conditioned stimuli acquiring positive properties (ref. 41, p. 401). On application of any of the conditioned stimuli, the animal entered into a state of pronounced excitation, which, as generally happens, was accompanied by severe hyperpnoea. The disuse of negative conditioned reflexes did not improve the condition of the animal. Hyperpnoea continued and the positive reflexes remained excessive. It was then resolved to use only those of the positive stimuli which were physiologically weak, i. e., the visual and tactile, and to discard the auditory, which as a rule in our experiments were strong. The beneficial

result of this treatment was immediate. The animal became quiet, hyperpnoea disappeared and the magnitude of the salivary effect returned to normal. This example and other observations suggested that a gradual development of internal inhibition in the cortex should be used for the reestablishment of the balance of normal conditions in cases of an unbalanced nervous system. The classical method consisted in the performance of so-called "passes"—weak, monotonously repeated tactile and visual stimuli, just as in our experiments upon animals. At present the more usual method consists in the repetition of some form of words, describing sleep, articulated in a flat and monotonous tone of voice. Such words are, of course, conditioned stimuli which have become associated with the state of sleep. (Hypnosis.) In this manner any stimulus which has coincided several times with the development of sleep can now by itself initiate sleep or a hypnotic state. The mechanism is analogous to the inhibitory chain reflexes which are similar to the positive conditioned chain reflexes (ref. 41, p. 405).

To sum up, Pavlov found in his observations of dogs that there were three different modes of reestablishment of extinguished conditioned reflexes. In the first, spontaneous recovery occurred after a longer or shorter interval of rest; such recovery was slow in developing, but stable. In the second, quick recovery was brought about with the help of reinforcement by the underlying unconditioned reflex. In the third, quick recovery was effected through the introduction of some extraneous reflex. "The recoveries in the last two instances were described as fundamentally differing from one another, since the former was not only rapid, but also stable, whereas the latter, though equally quick, was only temporary—vanishing with the disappearance of the extraneous reflexes." For example, the color of the hair of the mother or nurse, her facial expression and touch, her step, voice and postural tensions, the sight of certain places, of a cup or a spoon, any or all of these factors may influence the child's responses and its motor activity. A nursling fed day after day in a certain place at a certain time will not eat the same food if the circumstances under which he has been accustomed to being fed are suddenly changed. Even though he is fed in the same bed but in a different position, his head in the position of his feet, he may refuse to take his bottle. The smile at the sight of a parent, the opening of the mouth at the sight of a spoon and hundreds of similar examples can be taken out of the daily life of a child. And just as these stimuli may have a favorable effect on the child's mental and physical health, so also may they have an unfavorable effect and produce many and various functional disturbances.

COMMENT AND SUMMARY

It is an admitted fact that knowledge of what for the want of a more exact nomenclature is referred to as "functional disorders" is in a confused and chaotic state. Freudianism, Adlerism and the other introspectionist schools of psychology have failed to give satisfactory expla-

nations of the pathogenesis of these common functional disorders, nor do they offer the medical practitioner fundamental principles for their successful treatment. Clinical neurology and pediatrics are in the same predicament. The literature on this subject abounds with "case reports" based on the unproved assumption of a "neuropathic diathesis." One fact emerges from the literature published on this and allied subjects; namely, that if one is to attempt to put the treatment for these functional disorders of children on a permanent and specific basis, one must study by exact and objective methods the organism as a whole in relation to its natural environment. There is fast being accumulated through physiologic research a large amount of important data pertaining to the physiology of the nervous system which some day may find its way into the hands of the practicing physician. The investigation of the electrical skin resistance by means of the string galvanometer to determine the affective state of the organ, the use of muscle tonus as an index of the tension of the nervous system, the determination of the functional capacity of an organ or a system by objective tests and the application of the idea of "progressive relaxation" in the treatment for nervous hypertension are a few examples of the physiologic research in this field. Yet in none of these have definite principles been established for successfully coping with this problem.

Though all of the conclusions presented by this great physiologist, Pavlov, and his disciples may not be justified, and although some of their interpretations for clinical use may not be convincing, nevertheless, they have made a permanent contribution to the physiology of the nervous system and to clinical pediatrics. They have collected a mine of facts for a period of thirty years. They have observed by the most rigorous methods, to the most minute detail, the behavior of dogs under the most carefully controlled conditions and under the most varied circumstances. They have repeated their experiments hundreds of times, only to obtain the same results. They have followed the axiom of Aristotle, that the best way to study behavior is by observation. What Pavlov and his co-workers have so brilliantly accomplished through realistic and objective description and through systematic recording of facts pertaining to the behavior of animals, now remains to be done in the study of human behavior. There may be some who still view with skepticism the interpretations of this school, yet it seems to me that Pavlov's concept offers at the present time the most, if not the only, hopeful foundation for the understanding and treatment of functional disorders in children.

Dr. E. Heron of the University of Minnesota and Dr. W. H. Gantt of the Henry Phipps Institute of the Johns Hopkins Medical School made many valuable suggestions concerning this review.

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Pediatric Biographies

HEINRICH von LOUFFENBURG
1391–1460

JOHN RUHRÄH, M.D.
BALTIMORE

There are a number of exceedingly interesting pediatric poems that are important in the history of the diseases of children, as they give accurate information concerning the infant welfare work of the periods in question. By far the most practical is the pediatric part of the "Versehung des Leibs" published in 1491. This was written by a monk, Heinrich von Louffenburg, born, according to Baas, in 1391, at Louffenburg on the Rhein. In 1434, he appears as dean of the Mauritiustift in Zofingen; later he was in Freiburg, but in 1445, he entered the Johanniterkloster, "Zum grünen Werde," in Strassburg. He was still living there in 1458, and died on March 31, 1460. Most of his writing was done between 1415 and 1458. He left many manuscripts of songs, some popular as "Ich wölt, dass ich daheime wär," church compositions, translations of Latin church poetry into popular dialect and many poems for and about the Virgin Mary. He wrote an adaptation or translated the "Speculam humanae salvationis" entitled "Der Spiegel menschlichen Heils" and the "Opus figurarum" of Conrad von Alzey in der Pfalz as "Das Buch der Figuren."

"Versehung des Leibs" was written in 1429, as the author states, and the book printed in Augsburg in 1491. The author's name does not appear in the printed book but does on an acrostic in a manuscript copy in the Bayerischen Staatsbibliothek, in Munich. This was discovered by Karl Baas, in 1905; in it the author names himself as Heinrich von Louffenburg von Fryburg ein Priester. Baas, familiar with the incunabulum, identified the manuscript. The book is given in Panzer, no. 322, Hain 16017; Sudhoff notes it in his work on the German medical incunabula. Sudhoff also described an illustrated manuscript,[1] and Siegerist in the *Zeitschrift für Bücherfreunde* has given an account of another illustrated manuscript in the Zürcher Zentralbibliothek.

The back of the title page of the incunabulum contains a woodcut figuring God the Father; a rhymed table of contents follows. There

1. Sudhoff: Mitt. a. d. Geb. Med. u. Naturw. **15**:188, 1916.

Versehung des leibs

Dis büchlein ist also gemacht
wie dz jar nach dē monat wirt ge/
Nach natur vñ influß ō stern (acht
auch thůt es weiter lern
Von speiß tranck vñ purgieren
baden lassen vnd regieren
Schwäger frawē die fruchtber sind
wie man ziehen soll die kind
Vor ō pestilencz sich machen frey
darūb ist es ein būch ō arczney

Fig. 1.—First page of "Versehung des Leibs."

Das ward gedichtet sunderbar
do man zalt tausent jar
Vierhundert.xxix.jare me
gott behütte vns alle vor we
Und welle vns geben ewigklich
rūwe bey ime jm hymmelrich

Gedruckt czů Augspurg.
jn dem.lxxxxj.jare.

Fig. 2.--The end of the poem, giving the date of composition and printing.

Wievon die künste der maister gert
das des kindes rechte zeit
Zů seügend sy zwey jar
wie doch es gar dick fürwar
Entwenet wirt von milche ee
hie nach so sagent die maister me
Das man das kind entwenen sol
noch vnd noch das thůt jm wol
p iij

Fig. 3.—A page from "Versehung des Leibs" showing nursing bottle and pap bowl.

are seven chapters, the first of which contains a calender and before each month there is a woodcut showing the things most likely to happen in that month, and then follow in rime the precautions one should take to protect one's health during this month. The other chap-

Fig. 4.—Illustration from the Zürcher manuscript, showing the bath. (Courtesy of Professor Sigerist.)

Fig. 5.—Illustration from the Zürcher manuscript showing method of tying the child in the cradle. (Courtesy of Professor Sigerist.)

Fig. 6.—Portrait of the author—Zürcher manuscript. (Courtesy of Professor Sigerist.)

ters are on the seven planets, the nature of the twelve signs, an explanation of how the year is divided into four parts, also the four elements and the four complexions, the ordering of health, on pregnant women and the plague.

The author was evidently familiar with medical writers and medical practice, as well as the "Regimen Sanitatis" and the "Speculum Naturale of Vincenz, of Beauvais." The information imparted is not very unlike that given today excepting, of course, certain facts which have resulted from recent scientific investigation.

Maternal nursing is advised, but a wetnurse is used at first in case the mother's milk is unwholesome. Directions are given for weaning as well as bathing, dressing and general care. Louffenburg's successors added to his rather simple suggestions a number of the vagaries of the

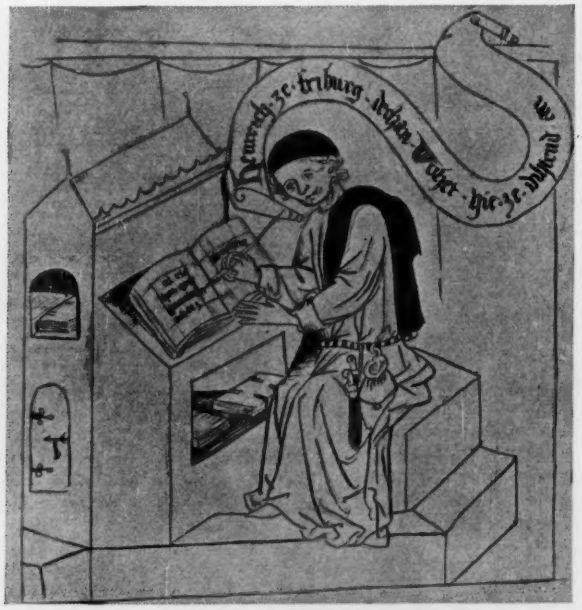

Fig. 7.—Portrait of the author—Strassburg manuscript. (Courtesy of Professor Sigerist.)

day, which after all are not unlike those which today at once amuse and irritate those in pediatric work.

The printed poem is illustrated with six woodcuts, all of which are reproduced in "Pediatrics of the Past," together with a partial translation of the 1491 edition and a full translation of that of 1544.

In the Zürcher manuscript there is a drawing of a scholar who is not mentioned in the text. Sigerist believes that this is a portrait of the author, especially as there is a similar illustration in the Strassburg manuscript, unfortunately destroyed by fire, but preserved in Engelhardt's reproduction.

A short section gives a good idea of the German infant welfare instruction of the fifteenth century:

HOW A MOTHER

must suckle and feed a child.

The Mother:

I feed and suckle my little child
according to its nature and need.
Nothing is more wholesome for children
in their early years than milk-food.
With this food you should nourish them
until they cut their teeth.
In case one gives them, before this time,
other food than milk,
they will become ill.
Another fact you must bear in mind,
namely, that no milk imparts more strength to the child
than the milk which it sucks from the mother.
Hence it should be delighted merely
to draw the breast of its mother.
On that it lives much better, and without harm,
than on the milk of any other woman.
However this the mother should know
that she must be just as careful
concerning eating and drinking, as formerly
when she was pregnant.
In order that the child may digest the milk well,
she should suckle it three times
or twice a day,
until it has gained sufficient strength.
And when it can digest better,
she should let it suckle frequently.
But not much at a time
that it may well digest the quantity imbibed.
The mother must likewise be careful
to remove in advance
her coarse milk every morning;
otherwise some harm might arise
if she allowed the child to suck it.
Nor should she hesitate,
in case her breasts are inflamed
and the child is anxious to suck,
to get another woman
to suckle it
until her own milk again becomes good
when she again should take care of it herself.
It is essential to let the child suck moderately
so that it may not overdo the sucking.
In case it has done too much sucking,

the mother's breast should be withheld from the child.
For great harm will ensue
if it has sucked too much.
But the sucking is also beneficial;
therefore the mother must often drink something.

THE LOUFFENBURG REPRINTS

There were apparently a number of reprints of Louffenburg's poem, which is considered in this article. Two of these at least were

14

Ein Regiment der ge-
ſundtheit / Für die jungen Kinder/
Wie ſie nach der Geburt bey geſundtem leibe er-
halten / mit Eſſen/Trincken/ Schlaffen baden ꝛc
Vnd von allerley zufelligen kranckheiten/
So jnen in der kindheit begegnen/
erlediget ſollen werden.

Plin

Gedruckt zu Franckfurdt am Mayn/
durch Herman Gülfferichen / in der Schmir-
gaſſen zum Krug
M. D. XLIX.

Fig. 8.—Title page of the 1549 edition of Metlinger and a rendition of the pediatric part of Louffenburg's poem "Versehung des Leibs."

issued together with a debased text founded on Metlinger's book. One of these was printed in 1532, at "Meintz" by Peter Jordan and is entitled: "Eyn Regiment der Gesundheit für die Jungen Kinder." There is a "Vorrede" in which the anonymous author states that it had been previously printed in "Eyn büchlein der frauen rosen gart genannt," which was the work of Eucharius Rösslein on obstetrics, first printed in 1513 at Worms, the standard authority on midwifery during the renaissance; of this book there are numerous editions, some

with Metlinger's work in which credit is given to that author, and some in which the text, more or less changed, has been used without stating its origin. There is also an edition of the pediatric poem printed in 1544, by Hermann Gulfferich in "der Schuurgassen zum Krug, in Frankfurt an Mayn."

Both editions are the same as to material but differ in format and illustrations. The subjects of the pictures are the same but they have been redrawn and are based on those in Louffenburg's poem.

Both books start with a "Vorrede" and a table of contents:

Information as to how pregnant women should be cared for.
How the new-born child is to be looked after.
How one shall bathe and put it to sleep.
How one shall feed and suckle it.
How it should be cared for when it teeths.
How the wet nurse shall be chosen.
How long children should nurse and how they should be weaned.
How the following diseases are to be cured. [There are thirty-five of these diseases. In Gulfferich's edition, the chapter "Für lemigkeyt der Kinder," or on paralysis of children, has been left out.]
Appendix. [This section, gives the German equivalents for the Latin names of plants.]

The following translation of a short section will give some idea of the style and material:

HOW THE CHILD MUST BE SWADDLED

and put to bed.

The Mother:

I keep my child quiet in a gentle manner / and wrap it up in cloths.
Now mark further what I say: / After the third or fourth day when its
navel falls off, / you should take egg-shells,
pound them to powder / and mix it well with wine.
Sprinkle with this mixture its delicate navel, / and then bind it firmly
in very clean cloths. / Stretch your child's arms and legs well.
Cover its head very thinly / or wind something round it neatly.
Also must the head lie higher than its body. / After that rock the child
to and fro, yet gently and noiselessly. / Sing also at the same time a sweet melody
in an undertone without much noise. / That will help the child in more than one way;
it will exhilarate its mind / and prepare it for sweet sleep.
Then when it is quite gently asleep / you must further look out
that the child will not be seized with fright. / Then put it in a quiet place
with its cradle, making no noise, / in a cool and dark place.
Cover the child's eyes / so that it may not see the daylight.

In this way its eyes will gain strength. / When afterwards it awakes from its sleep,
it is best to turn its eyes / towards daylight.
After that a bath will be wholesome for the child; / you ought to bathe it
so long until its body / shows a red glow; then it is time
for the child to be taken out of the bath. / But mark also this advice:
the water shall only be lukewarm. / Afterwards rub it gently with honey.
Then, wash without soap / its ears and eyes clean;
after then wipe it with clean cloths. / Finally you should also carefully
anoint the child with sweet oil / all over its body.
Then you should also bend its limbs / to and fro, up and down:
legs, neck, back, hands, / arms, sides and loins,
as you wish them to be shaped: / such a proceeding will prove beneficial in many respects.

Pediatrics in Art

POLIOMYELITIS?

JOHN RUHRÄH, M.D.
BALTIMORE

This portrait of a young prince of the eighteenth dynasty of Egyptian rulers (1580-1350 B. C.) shows a deformity of the right leg which is frequently referred to as illustrating an early case of poliomyelitis. It might, however, be due to some other lesion in the nervous system or to a disease of the hip joint contracted in infancy. The portrait is of Ruma, and his wife Imoa, both Syrians, and their child. Ruma had charge of the temple of Astarte in Memphis, from which the stele doubtless came (Hamburger, O.: *Bull. Soc. franç. d'hist. de la méd.* **10:** 407, 1911). Another possible illustration of poliomyelitis is the talipes equinus shown in the mummy of the Pharaoh Siptah of the nineteenth dynasty, who died 1209 B. C. (Smith, G. E.: The Royal Mummies, Cairo, 1912). The portrait above is taken from a small colored stele, 27 by 18 cm., in the Carlsberg Glyptothek, Copenhagen. (Courtesy of the Carlsberg Glyptothek.)

News and Comment

GENERAL

Pamphlets on Nutrition.—The American Child Health Association has published two pamphlets: Food at Low Cost, by Lucy H. Gillett, and Emergency Nutrition, by Henry C. Sherman. These are published to meet the essential needs at the present time. They may be obtained from the American Child Health Association at the following rates: from 10 to 25 copies at $0.01 each, from 25 to 99 copies at $0.0075 each; from 100 to 499 copies at $0.006 each and 500 or more copies at $0.005 each. These prices include transportation.

UNIVERSITY NEWS

Tulane University of Louisiana, School of Medicine, New Orleans, has announced the appointments of Dr. Frank James Kinberger as assistant professor of clinical pediatrics and Dr. Jack Erell Strange as clinical assistant in pediatrics.

The Faculty of Medicine of Montevideo has conferred on Dr. Jules Comby of Paris the title of Honorary Professor.

Dr. Ivo Nasso, of the chair of pediatrics of Messina, replaces Dr. C. Cattaneo, deceased, in the pediatric chair at Milan.

Dr. Salvatore Maggiore, from the Pediatric Clinic of Bari, replaces Dr. Nasso at Messina.

Dr. Gino Frontali has been named professor of the Pediatric Clinic at the University of Padua.

Dr. G. Fanconi of the University of Zurich has taken the place made vacant by Prof. E. Feer, who retired after a long, brilliant career.

PERSONAL

The eminent Uruguayan professor of pediatrics, Dr. Luis Morquio, has recently been made an Officer of the Legion of Honor by the French Government.

SOCIETY NEWS

American Orthopsychiatric Association.—The ninth annual meeting of the Association will be held at the Lord Baltimore Hotel in Baltimore, Feb. 18, 19 and 20, 1932. Dr. Ralph P. Truitt is chairman of arrangements.

CORRECTION

In the article by Dr. I. Newton Kugelmass and Ethyl Greenwald, entitled, "Phospholipids in the Blood in Infants and in Children," in the November issue (**42**:1134, 1931), the word "centimeters" in the second line of the first conclusion, on page 1136, should read "milligrams."

Abstracts from Current Literature

Anatomy and Physiology

IRREGULAR HEART ACTION IN CHILDHOOD. ALBERT PEIPER, Deutsche med. Wchnschr. **56**:1079 (June 27) 1930.

Respiratory arrhythmia is a sinus arrhythmia; it is common among children, and might be considered as normal. On the other hand, opinions are varied as to the significance of extrasystoles, which occur less frequently among children than among adults. Visco found 48 cases among 1,000 children who gave no evidence of organic heart disease. J. MacKenzie attributed no significance to extrasystoles in children. Nobécourt found temporary extrasystoles after excitement and in neuro-arthritism, anemia, convalescence from various diseases, hysteria and chorea. Even extreme mental work may produce temporary extrasystoles. Freiberger found auricular extrasystoles more frequent, whereas Hecht thinks that the ventricular type is most common. However, both of these authors realize that extrasystoles do not necessarily mean disease of the heart muscle. With the exception of Bass' cases, the cases presented in the literature were not followed sufficiently long for definite conclusions to be drawn. Peiper describes the cases of 12 patients who frequently showed extrasystoles. The ages ranged from 3 to 14 years. The male sex predominated. In all the cases, the extrasystoles were chance findings; the maximum time of observation was four and one-half years. Eleven of the 12 children remained free from lesions of the heart. In one of them rheumatic fever developed. The onset of the extrasystoles among the twelve children had no relationship to contagious diseases, and the constancy of the extrasystoles varied in the different children. Auricular extrasystoles were in the minority. The author concludes that the presence of extrasystoles among children has no significance, demands no treatment and has no bearing on the present and future condition of the developing heart.

KERESZTURI, New York.

ROENTGEN EXAMINATION OF THE SIZE OF THE HEART IN CHILDHOOD. FRITZ VON BERNUTH, Ergebn. d. inn. Med. u. Kinderh. **39**:69, 1931.

The author says that theoretical considerations led him to recognize that the size of the heart can best be expressed in relation to the general body structure. Since the build of the body cannot be characterized by one measure, such as height, it becomes necessary to employ also another unit, namely, the width of the body. By empiric methods the author arrived at a formula expressing the cardiac relationship, namely:

$$\frac{\text{Height} \times \text{transverse diameter of the lungs (taken at their widest portion, i. e., near the peak of the diaphragm)}}{\text{Cardiac surface (measured by an orthodiagram)}} = \text{from 31 to 47}$$

When the quotient is less than 31, one must assume that an enlargement of the heart is present; if it is greater than 47, one is dealing with a relatively small heart. These values hold good for pictures taken at a distance of 1.5 meters. Instead of "cardiac surface" one may employ the "cardiac right angle," obtained by multiplying the length and width diameters of the heart; in that case the quotient lies between 23 and 35. The quotient remains the same throughout childhood, which makes it extraordinarily useful. Only during infancy, the values are somewhat smaller, namely, from 29 to 44 and from 22 to 33, respectively. That is due to the well known fact that the heart at that age is relatively larger than later in childhood. The quotient does not change in puberty.

The author found this quotient very applicable in practice. Hearts with a quotient below 31, he found definitely enlarged — except during earliest infancy. He was also able to show that hearts that had heretofore been considered enlarged were normal in size when measured according to his formula.

Finally, he warns against a too dogmatic interpretation of the formula in relation to the size of the heart. He says that undoubtedly there are pathologically enlarged hearts, especially at the incipiency of the enlargement, in which the quotient may still be normal. In such cases, the roentgen observations must be evaluated in conjunction with the clinical picture.

CAPPER, Philadelphia.

Pathology, Bacteriology and Biochemistry

MOLECULAR WEIGHT OF CASEIN. T. SVEDBERG, L. M. CARPENTER and D. C. CARPENTER, J. Am. Chem. Soc. **52**:241 (Jan.) 1930.

Casein prepared by the Hammarsten method has been examined at p_H 6.8 in phosphate buffer solution by the centrifugal sedimentation velocity method and found to consist of a mixture of protein molecules of different weights. Hammarsten casein was extracted with hot acidified 70 per cent ethyl alcohol and the soluble protein precipitated out with dilute sodium hydroxide. This protein after washing was dissolved in a phosphate buffer solution of p_H 6.8. Various concentrations were examined by both the sedimentation velocity and sedimentation equilibrium methods. Within the limits of experimental error the acid ethyl alcohol soluble protein was found to be homogeneous with regard to molecular weight. It is therefore a pure chemical individual. The molecular weight was $375{,}000 \pm 11{,}000$. The molecule was not spherical and deviated from the spherical shape by about the same amount as that found for several other proteins.

KUGELMASS, New York.

PRELIMINARY REPORT OF COMMITTEE ON MILK PRODUCTION AND CONTROL, WHITE HOUSE CONFERENCE, Pub. Health Rep. **46**:769 (April 3) 1931.

The committee concludes that an adequate supply of safe milk of good quality should be available for all children. There is need for further improvement in the supervision of the milk supply of this country. Laws or regulations for the supervision of milk supplies, whether local, state or federal, should incorporate uniform requirements at least equivalent to those contained in a milk ordinance to be recommended by the United States Public Health Service and the Bureau of Dairy Industry of the United States Department of Agriculture.

SANFORD, Chicago.

BACTERIOLYSIS OF THE TUBERCLE BACILLUS: SIGNIFICANCE OF GRANULATION. FERNAND BEZANÇON and ANDRÉ PHILIBERT, Rev. de la tuberc. **12**:223 (March) 1931.

Koch's bacillus is extremely resistant to all destructive agencies in nature and in culture. It does not undergo autolysis, and it retains its vitality for months and years. Granulation does not indicate a bacteriolytic action, but is a natural phenomenon, especially in old cultures and in tuberculous tissues where there is little tendency to growth and where young forms are scarce. In old cultures granulation forms and free granulations are often found from which positive cultures are easily grown. Granulations indicate resistance and not bacteriolysis. The significance of partial or complete loss of acid-resisting qualities on the part of the tubercle bacillus is not thoroughly understood. It may be said, however, that the loss or lack of acquisition of this character is not indicative of bacteriolysis.

SMITH, Ogden, Utah.

BACTERIOLYSIS OF THE TUBERCLE BACILLUS IN THE BODY FLUIDS. F. BEZANÇON and E. BUC, Rev. de la tuberc. **12**:244 (March) 1931.

The possession of bacteriolytic properties by pleural effusions has not been demonstrated. Cultures and the injection of infected fluid into animals at all stages of development showed the presence of numerous bacilli. This was true of pneumothorax fluids and of old and recent exudates.

SMITH, Ogden, Utah.

BACTERIOLYSIS OF TUBERCLE BACILLI IN THE TISSUES. JEAN PARAF, Rev. de la tuberc. **12**:266 (March) 1931.

In the healthy receptive animal, in the refractory animal and in the tuberculous animal, the defensive mechanism against the tubercle bacillus is the same. In all three cases it consists of tentative walling off and elimination of the bacillus on the one hand and of destruction or lysis on the other. The phenomena, incomplete in the healthy receptive animal and more marked in the refractory animal, attain their maximum in the reinfected tuberculous animal. These defensive properties do not lie in the body fluids, but entirely in the large mononuclear cell of connective tissue origin, which is a veritable antibacillary macrophage. This is the only body cell capable of destroying the tubercle bacillus. This lytic property, up to the present time, cannot be transmitted to another animal since it appears to reside entirely in the activity of the cells themselves.

SMITH, Ogden, Utah.

THE FREE AND COMBINED BLOOD SUGAR IN INFANCY. ALFREDO LUCCA, Pediatria **39**:681 (July 1) 1931.

Sixteen healthy infants, of whom eleven were nurslings, were studied in this series. Estimations of blood sugar values made during hunger (sixteen cases) gave the same results for free sugar as those generally obtained in adults, namely, from 0.75 to 1.06 per cent, while the combined sugar gave figures varying between 0.37 and 0.51 per cent. In acute disorders of the digestive tract there prevailed an increase in the percentage of the free sugar proportionate to the severity of the disorder, reaching as high as from 1.36 to 1.41 per cent. At the same time there appeared a parallel increase in the combined sugar. In chronic disorders of the digestive tract the free sugar was found to remain within the normal limits, namely, from 0.70 to 0.75 per cent. This normal or near normal content also applied to figures representing the combined sugar.

In five normal infants, estimates made following the hypodermic administration of dextrose showed an appreciable increase of free sugar within ten to fifteen minutes and a return to normal within one and one-quarter to one and one-half hours. The effects on the combined sugar in these cases was either nil or a slight decrease with a return to normal within one and one-quarter to one and one-half hours.

SIGNORELLI, New Orleans.

THE MODIFICATIONS OF CALCIUM, POTASSIUM AND PHOSPHORUS IN THE SERUM AS A RESULT OF INJECTION OF A SALT OF CALCIUM, POTASSIUM AND PHOSPHORUS. V. ZAMORANI, Riv. di clin. pediat. **29**:285, 1931.

Rabbits and dogs were used in these observations. The injection of 2 cc. of a 5 per cent solution of calcium isobutyrate per kilogram of body weight intravenously caused an increase in the calcium and phosphorus and a decrease in the potassium of the blood serum. The injection of 40 mg. of a 3 per cent solution of potassium chloride per kilogram of body weight did not appreciably affect the calcium or potassium, but did decrease the phosphorus of the blood serum. The intravenous injection of 0.15 Gm. of acid sodium phosphate in a 10 per cent solution increased the phosphorus and diminished the calcium and potassium of the blood

serum. The intravenous injection of from 0.1 to 0.2 Gm. of trisodium phosphate in a 10 per cent solution increased the potassium and phosphorus, and decreased the calcium of the blood serum.

HIGGINS, Boston.

BONE CHANGES PRODUCED BY VIOSTEROL IN ANIMAL EXPERIMENTS. M. SCHMIDTMANN, Virchows Arch. f. path. Anat. **280**:1 (Feb. 4) 1931.

The author has studied the anatomico-histologic changes produced by administration of irradiated ergosterol (viosterol) to young and adult rats, rabbits and cats. Collazo and Schmidtmann had found that in young rats, large doses of viosterol caused a cessation of growth, certain irregularities in the structure of the resting cartilage and a lack of proliferative cartilage at the epiphyseal line (dwarfed rats). In animals that were normal, rachitic or that received rickets-producing diets with the addition of viosterol, these changes were found in all young animals after the administration of viosterol: hyperemia of the bone marrow with invasion of the capillaries into the proliferating cartilage of the epiphyseal line, a marked decrease in the size of the proliferating cartilage zone and calcification of the matrix of the proliferating cartilage. Additional feeding of calcium was associated with a decrease in weight and calcification of the walls of the blood vessels and heart muscle.

In adult animals bone changes could not be regularly observed. Two types of changes were present. After the administration of viosterol for a short time the calcium content of the bone was increased with a broadening of the trabeculae and of the corticalis. Later, especially in rabbits, severe damage was present. A softening and thinning of the bones caused by a slow transformation of the compact corticalis into spongioid bone which became more and more poor in calcium and liable to spontaneous fractures.

The author concludes that changes in the bones and in the blood vessels are caused by the same noxa. The histologic picture produced by the administration of viosterol is different from that seen in normal bone or in rachitic bone healing spontaneously. The author is inclined to accept Pfaundler's view that irradiated ergosterol has not the character of a vitamin, but forms a barricade against the rickets-producing factors.

SCHOENTHAL, New York.

THE CENTER OF EPINEPHRINE SECRETION AND NERVE CONTROL OF BLOOD SUGAR REGULATION. GABRIEL MONASTERIO, Wien. Arch. f. inn. Med. **21**:451 (July) 1931.

The epinephrine secretory center has the function of a blood sugar regulatory center. It belongs to the Claude Bernard bulbar center, which also regulates glycogenolysis in the liver. The two centers, the epinephrine secretory and the glycogenolytic, are united as a common center in this structure, and must be regarded as the sugar-regulating center. The moment the blood sugar declines, this center liberates sugar in the liver through the process of stimulating glycogenolysis, either indirectly by flooding out epinephrine or directly by stimulation of the splanchnic nerves leading to the liver.

SCHLUTZ, Chicago.

THE ACTION OF ULTRAVIOLET RAYS OF THE HUMERAL METABOLISM IN THE PATHOLOGIC AND NORMAL STATE. ENACHESCU and DANULESCU, Spitalul **51**:213 (May) 1931.

The authors administered ultraviolet rays to adults and debilitated infants (hypotrophic and rachitic). In testing the cholesterol calcium and reserve alkali of the blood before and after irradiation, they obtained the following results: There are no important modifications of the calcium and reserve alkali in adults; in contrast, the cholesterol is noticeably increased from one to two hours after the ultraviolet irradiation. This increase attains, in general, its maximum during

the erythematous period. In children the ultraviolet rays may increase not only cholesteroluria but also the calcium of the blood and the alkaline reserve. These modifications are more appreciable in hypocalcemic-rachitic and slightly acidotic conditions.

AUTHORS' SUMMARY.

NEWER RESEARCHES ON ERGOSTEROL. PAUL BAUMRETTER, Pediatria Polska **10**:26 (Jan.-Feb.) 1930.

The author reviews the work of European and American investigators on the action of ergosterol, and concludes that ergosterol is a very potent drug which most of the workers admit produces poisoning when given in larger doses. They have not come to any conclusion as to what factor in ergosterol produces poisoning. The author states that the drug must be under the strict control of the physician.

KRUPINSKI, Chicago.

INJURIES, PARTICULARLY OF THE HEART, CAUSED BY ANTIRACHITIC AGENTS: II. THE ELECTROCARDIOGRAM IN WHITE MICE AND RABBITS TREATED WITH VIOSTEROL. NILS STENSTRÖM, Acta pædiat. **10**:577 (June 30) 1931.

Mice treated with viosterol showed electrocardiographic alterations similar to those previously reported by Agduhr and Stenström. When rabbits were used, the controls showed definite electrocardiographic and anatomic changes, and the rabbits given cod liver oil showed less marked changes than those reported by Agduhr and Stenström. The group given viosterol showed prolongation of the auriculoventricular conduction time and of the Q-R-S interval, as had those previously studied which were given cod liver oil. The author infers that the injurious effect of these various antirachitic agents is closely related to the active principle.

MCINTOSH, New York.

A RAPID METHOD OF DEMONSTRATING DIPHTHERIA BACILLI. V. KENT, Ugesk. f. læger **93**:690 (June 25) 1931.

Portions of diphtheritic membranes fixed on slides and stained with Bie's fluid gave positive results in 79 per cent of cases. This method should be of value in bedside diagnosis. It indicates the importance of the early use of antitoxin.

ELGHAMMER, Chicago.

Nutrition

ACTIVATED ERGOSTEROL IN RADIATION SICKNESS. LESTER A. SMITH, Am. J. Roentgenol. **22**:317 (Oct.) 1929.

The clinical picture of radiation sickness may be (1) immediate, consisting of malaise, loss of appetite, headache, vomiting, fever, diarrhea or acute prostration, or (2) late, with nausea, abdominal pain and distention, fever, diarrhea, general weakness and fatigability or even cachexia. The theories are: (1) toxemia from broken-down proteins or lecithin lipoids, (2) a decrease in the cholesterol content of the blood, (3) a shift of the body chlorides, (4) an alkalosis and (5) an increased vagus tonus. The oral administration of activated ergosterol produced marked relief of all symptoms, except possibly the diarrhea. Used as a prophylactic, ergosterol prevents all symptoms to a marked degree, the same results occurring apparently in both radium and roentgen treatment. Many of the patients experience an unusual sense of well-being and increased appetite. The action is probably effected in some way through the calcium-phosphorus metabolism. There is some evidence that the final effect may be brought about through the prevention or reduction of hyperirritability of the vagus. A bibliography is appended.

STULIK, Chicago.

COEFFICIENTS OF DIGESTIBILITY OF THE CONSTITUENTS OF MILK AND THE BALANCE OF CALCIUM AND PHOSPHORUS IN CALVES ON A MILK DIET. J. S. HUGHES and H. W. CAVE, J. Nutrition **4**:163 (July) 1931.

Two calves were restricted to a milk diet for a period of about eight months. The animals were not allowed roughage in any form. The results of the experiment revealed that the ability of the calves to digest food was not impaired by restricting them to this diet. Roughage plays a part in the development of the muscles of the paunch and intestines. The authors' results indicate that this development is not necessary for the secretion of digestive juices.

MUNNS, Winnetka, Ill.

THE EFFECT OF MINERAL OIL ADMINISTRATION UPON THE NUTRITIONAL ECONOMY OF FAT SOLUBLE VITAMINS: I. STUDIES WITH THE VITAMIN A OF BUTTER FAT. R. W. JACKSON, J. Nutrition **4**:171 (July) 1931.

The work was conducted with rats as experimental animals. The author found that mineral oil caused a considerable loss of vitamin A provided the mineral oil was mixed with the vitamin prior to ingestion. When mineral oil was administered separately there was only slight diversion of vitamin A. A moderate increase of the vitamin A-containing food—in these experiments, butter fat—appeared to protect the animal from vitamin A deficiency when mineral oil was given separately.

MUNNS, Winnetka, Ill.

THE EFFECT OF PASTEURIZATION UPON THE VITAMIN C CONTENT OF MILK IN THE PRESENCE OF CERTAIN METALS. E. W. SCHWARTZE, F. J. MURPHY and GERALD J. COX, J. Nutrition **4**:211 (July) 1931.

Guinea-pigs that were placed on scorbutic diets were fed whole cow's milk that had been pasteurized under aerobic conditions in copper, tin-plated copper and aluminum vessels. The results indicate that from 80 to 90 per cent of the vitamin C was destroyed when milk was pasteurized in naked copper containers; only from 20 to 40 per cent of vitamin C was destroyed when tinned copper containers were used, and somewhat less than from 20 to 40 per cent when the containers were of aluminum. These figures indicate that copper is unsuited for the construction of dairy equipment if one desires to conserve vitamin C.

MUNNS, Winnetka, Ill.

FURTHER OBSERVATIONS ON THE EFFECT OF LIGHT ON THE SYNTHESIS OF VITAMINS. V. G. HELLER and RUTH R. ST. JULIAN, J. Nutrition **4**:227 (July) 1931.

The specific problems in this particular work are to determine: (1) the effect of colored lights on the synthesis of vitamin A; (2) the effect of blanching tissue that has previously become potent; (3) the possible migration of the vitamin from one portion of the plant to another, and (4) the effect of light on the synthesis of vitamin D.

The first problem could not be fully answered. The results indicate that the short wave length is more important and that light waves beyond the spectrum are also effective. The results of the second experiment indicate that blanching does not destroy the vitamin potency of green leaves which, through exposure to sunshine, have become a good source of vitamin. The vitamin seems to be stored in the portion of the plant most exposed to the sunlight, and is not transferred to other portions of the plant. There seems to be no relationship between vitamin potency and color in vegetables. Light seems to have little effect on the synthesis of vitamin D in vegetables, and they are a poor source of that substance.

MUNNS, Winnetka, Ill.

FAT SOLUBLE VITAMINS: XXXII. THE DISTRIBUTION OF VITAMIN A IN TOMATO AND THE STABILITY OF ADDED VITAMIN D. H. STEENBOCK and INEZ M. SCHRADER, J. Nutrition **4**:267 (July) 1931.

The tomato is generally recognized as a potent source of vitamins A, B and C. Steenbock and Schrader, after experiments on rats in which ophthalmia had been produced by a deficiency diet, concluded that the pulp of ripe red tomatoes from which the skin and seeds had been removed contains approximately thirty-two times as much vitamin A as the clear yellow serum. These results indicate that from a nutritive standpoint filtered juice is much less preferable than a juice containing the pulp in suspension.

Vitamin D added to tomato juice in the form of ergosterol maintained its activity after sterilization and storage for thirteen months at 37 C.

MUNNS, Winnetka, Ill.

THE SPECTRA AND ANTIRACHITIC POTENCIES OF VARIOUS "THERAPEUTIC" LAMPS. ELIZABETH M. KOCH, F. C. KOCH, I. S. FALK and H. B. LEMON, J. Prev. Med. **5**:187 (May) 1931.

This is an interesting and detailed report which may be summarized as follows: "1. Radiations of significant intensity in the physiological region (3,100-2,900 angstrom units) have been demonstrated by the spectrographic examination of the following lamps: (*a*) tungsten-filament, incandescent, gas-filled, in bulbs made of glass with high transmission coefficients for ultra violet light in region 3,100-2,900 angstrom units; (*b*) carbon arc using "sunshine" carbons equipped with a filter of similar material; (*c*) mercury-vapor lamps in bulbs of glass reducing the intensity below 2,900 angstrom units; (*d*) low-pressure arcs of the two following types: 'Pointolite' (a nitrogen arc in a bulb of glass transmitting ultra violet), and the General Electric type, a mercury-vapor arc between tungsten blocks enclosed in a bulb of similar material.

"2. From a comparison of the spectrographs of these lamps with those of summer sunlight, whose antirachitic potency is attested by wide clinical experience, it appears that these lamps should possess significant antirachitic potencies.

"3. The spectrographs of some of these lamps, however, indicate that there has not been sufficient reduction of the short wave lengths to place them in the group of so-called 'sunshine' lamps.

"4. Direct tests with albino rats maintained on an intensely rickets-producing diet demonstrate the definite antirachitic potencies of all these lamps, evaluated either on an absolute basis or by comparison with a powerful mercury-vapor quartz lamp. These results are the more significant because the conditions of the rat test are extreme.

"5. Further experimentation with incandescent lamps as sources of ultra violet radiations of moderate intensity, delimited to wave lengths that do not far exceed the lower limits of sunlight (at ground level), shows that such lamps have the obvious advantages of safety, convenience and moderate cost. They require, however, a very long exposure time."

TURNER, Chicago.

VOMITING IN INFANCY. S. J. BARNETT, Northwest Med. **30**:129 (March) 1931.

Barnett reports the use of phenobarbital combined with thick cereal feeding in hypertonic, colicky, vomiting infants. He gives from one-eighth to one-fourth grain (125 to 250 mg.) at each feeding. He observed no evidence of idiosyncrasy in either skin effects or cumulative action. The dosage is gradually reduced. The clinical effects are striking.

SCOTT, Philadelphia.

FOOD ALLERGIES IN CHILDREN. HELEN G. DENNIS and C. ULYSSES MOORE, Northwest Med. **30**:267 (June) 1931.

Dennis and Moore comment on the frequency with which retests are positive. They believe that a persistent dislike for a food may have an allergic basis. Most of their cases showed more than one form of allergic disease. They believe that about 300 tests are necessary, about 20 to be done at one sitting. They use the scratch test.

SCOTT, Philadelphia.

SOME MINOR DIGESTIVE DISORDERS IN BREAST FED INFANTS DURING THE FIRST MONTH. CHARLES MCNEIL, Edinburgh M. J. (Tr. Obst. Soc.) **38**:72 (June) 1931.

During the first four weeks of life breast-fed babies have certain digestive disturbances which are common. These may be made the occasion for weaning the infant. Contrary to such a practice, there is a tendency, while emphasizing the desirability of breast feeding, to underestimate these difficulties which can and do arise in the new-born infant. This is found in textbooks and medical teaching. Faulty food and a functional disturbance in the child's digestion are the sources of the disorders. The author does not include any organic disease or congenital defect. There is an absence of exact knowledge in regard to dyspepsia in the new-born infant. McNeil suggests the following clinical groups: (1) mild diarrhea with green and frequent stools, a very common condition; (2) a fairly common, special type of vomiting; (3) a not uncommon special type of constipation, and (4) failure to gain weight without any other dyspeptic symptoms; there are a number of different types of cases in this group which are very important, the characteristic of all being the failure to gain weight without real dyspepsia.

All these conditions are trivial at the outset, beginning usually about the end of the first week. The first three groups may be accompanied by an increase in weight for several weeks, to be followed by other symptoms of dyspepsia. Mother's milk is blamed for it usually, and if the symptoms persist or become aggravated, especially with loss of weight, the baby is taken away from the breast. McNeil thinks that the first three groups are definite types of functional disorder produced by a disturbance in the muscular apparatus of digestion. This consists of a maladjustment between peristaltic action and sphincter control. He discusses the behavior of colostrum and mature milk when they reach the stomach and intestines; the phenomenon of regurgitation, due to the inaction of the so-called cardiac sphincter, becomes more violent and represents real vomiting when the pyloric sphincter goes into spasm. When in the first week of life the stomach is filled with fluid food it is necessary that the mechanical arrangements of contraction and relaxation be brought into full activity.

The same condition of a contractile reservoir, guarded by a sphincter, exists in the lower bowel, so that the anal sphincter which is normally open three or four times a day may become more sensitive and permit frequent evacuations of the stool or undergo spasm and lead to constipation.

Green and frequent stools are common in breast-fed infants. The condition is compatible with good health and digestion, but is an indication of unstable equilibrium. As it goes along, the stools become frothy and no longer uniform, containing masses of fatty soaps and visible mucus, and the buttocks are red and irritated. The baby becomes fretful and may lose a little weight; vomiting and colic appear, the sum total being a state of true dyspepsia. It has been caused by a temporary excess of milk and a slight increase of peristalsis with a high percentage of sugar in the milk, the fermentation of which increases the already active peristalsis.

If this condition continues for a few days, treatment may be necessary. Reduction in the number of minutes at the breast, a small dose of castor oil and a little mercury with chalk and alkali, will usually permit the baby to get well. The author believes that when further treatment is needed, good results come from

one-half teaspoonful doses of simple petroleum emulsion well diluted with water given twice daily. He advises against putting any laxative into the emulsion.

Vomiting is one of the commonest occurrences in young infants, and the special type of which McNeil treats is more often seen in girls. It is frequent, copious and explosive, coming on soon after nursing. The infants are impatient, nervous and irritable. This is probably due to pyloric spasm, or to an incoordination between the gastric peristalsis and pyloric action. The treatment is regular three-hour feeding, and slow nursing at the breast with interruptions to permit eructation of air. The child afterwards is quietly laid down and not dandled by the attendants. Sodium citrate may be given to good advantage, as well as a half grain (32.4 mg.) of chloral hydrate three times a day. There is no progressive wasting in these cases, and the babies should not be weaned.

The special type of constipation that McNeil discusses comes on toward the end of the first month and is due to anal spasm. Accompanying it is redness or scoring of the anal orifice. Vomiting and dyspepsia may come on later. The mother is instructed to dilate the anus once or twice daily, using the little finger anointed with a soothing preparation such as 5 per cent sulphonated bitumen N. F. in petrolatum. This should be kept up for a week. NEFF, Kansas City, Mo.

THE "VITAL" FACTOR IN DIET: THEORY OF NATURE OF VITAMINS. CHALMERS WATSON, Edinburgh M. J. (Tr. M.-Chir. Soc.) **38**:91 (June) 1931.

After eighteen years of intensive investigation, vitamins have never been isolated, so that it is not known whether they are merely properties or substances. The author attempts a hypothesis regarding the nature of vitamins. It is based on various data collected from personal observations. As long as twenty-five years ago, Watson studied in the physiological department of Edinburgh University the effect of certain diets on rats. He came to the conclusion then that the unfavorable symptoms observed were due to the premature loss of vital function, especially that factor which is concerned in warding off bacterial infection. When bread and milk had been added, the dietary contained specific beneficial vital properties which are now regarded as vitamins.

Properly irradiated milk has a pronounced curative action on rickets, due to a specific action whereby its nutritive value is increased. Mrs. Mellanby's researches for the Medical Research Council have shown that the activity of milk is greatly increased when irradiated. Irradiated medicinal substances may lose their power of curing rickets, but irradiated milk is taken fresh. It may contain more beneficial factors than vitamin D alone. No unfavorable results from irradiated milk have been learned from its extended use for several years.

The therapeutic value of a diet recommended by Dr. Gerson in Germany during the past few years is discussed. Watson took the opportunity of watching at first hand the effect of the Gerson diet, and has since tried it at the Royal Infirmary with favorable results. The diet consists of fresh fruit and vegetable juices, lactic acid milk and curds, oil used in cooking, potatoes cooked in their skins and restriction of meat. Salts are obtained from vegetables, no sodium chloride being allowed. The diet is a highly vitaminized therapeutic measure, producing vital energy not expressible as calories, the latter being simply heat energy.

The author deals finally with the electromagnetic field and the waves that have therapeutic value. The ultraviolet rays are concerned with nutrition, giving a chemical vital energy to promote the growth of the vegetable tissues which are to be consumed by animals or man. In nature, vitamins are found in the vegetable kingdom alone, from which they are imparted to animal tissues and milk. Solar energy acts on the plant cells to further the healthy state and progress of the plant. When the vegetables are eaten, this energy is passed along to animals. The special vitamin present in a particular plant may be produced in a manner that is analogous to the selective power by which the plant develops its particular color.

Living food is therefore the surest source, because it is nearest to the origin of its energy. Watson believes that the energy value of food should be studied in relation to its sunlight properties.

NEFF, Kansas City, Mo.

CRITICAL REVIEW: THE METABOLISM OF CALCIUM AND PHOSPHORUS AND THE PARATHYROIDS IN HEALTH AND DISEASE. DONALD HUNTER, Quart. J. Med. **24**:393 (April) 1931.

The author presents in an able manner a detailed review of the literature concerning calcium and phosphorus metabolism. The material is presented in such a way as to be readily accessible to the clinician. A bibliography of 202 references accompanies the monograph. The work is presented under the following subheadings: Introduction; Normal Metabolism of Calcium; Normal Metabolism of Phosphorus; Phosphatases; Effects of the Parathyroid Hormone; Parathyroid Tetany; Source of Available Calcium; Generalized Osteitis Fibrosa of von Recklinghausen; Focal Osteitis Fibrosa; Hematogenous Myelomatoses; Effects on Calcium Metabolism of Thyroxin and Thyroid Disease; Irradiated Ergosterol; Rickets; Osteomalacia; Antenatal Rickets; Influence of Diet on the Structure of Teeth; Hunger Osteopathy; Styfsiekte or Stiff-Sickness of Cattle; Late Rickets; Osteitis Deformans; Osteogenesis Imperfecta; Otosclerosis; Storage and Excretion of Lead; Use of Calcium Salts in Therapeutics; Bibliography.

BRADFORD, Rochester, N. Y.

EFFECT OF ULTRAVIOLET IRRADIATION ON THE LACTATING BREAST. E. LESNÉ and G. DREYFUS-SÉE, Nourrisson **19**:90 (March) 1931.

Daily irradiation of the breasts alone was practiced, beginning with five minutes and increasing to thirty-five minutes. The nipples were protected with petrolatum. For the effect on the quantity of milk secreted, fifteen mothers were treated. Increased lactation was obtained in ten; no increase in five. The amount of increase in some cases was not striking. As regards qualitative changes, no constant results were produced.

Breast milk normally contains very little vitamin D. Other investigators have shown that generalized exposure of nursing mothers increases the antirachitic potency of their milk. The authors have conducted experiments, using white rats as test animals, to prove that in nursing mothers exposure of the breasts will raise the vitamin D content in the milk secreted to such an amount that only 2 drops of this milk are required to prevent rickets in rats, whereas 8 drops from a mother who receives no irradiation will not give protection. The mechanism is not understood, but is believed to be due to a special exciting action on the skin covering the mammary glands.

MCCLELLAND, Cleveland.

ACIDITY OF THE STOOLS. H. DORLENCOURT and R. LAVANDON, Nourrisson **19**: 147 (May) 1931.

Breast-fed infants have acid stools with a p_H varying from 5.5 to 6.4. Infants fed on cow's milk have neutral or alkaline stools (p_H 7.2). Buttermilk also produces stools that are either neutral or slightly alkaline. A change from breast milk to cow's milk produces rapid alteration of the stools to the alkaline side. The age of the infant is immaterial.

The stools of infants with simple diarrhea become acid. In the severe types of choleriform diarrhea this acidity becomes much more acute, with a p_H as low as 5.0. Acute infections vary in the effects that they produce, though the general tendency is toward an acid stool. There is no relationship between the nature and severity of the infection and the degree of stool acidity.

The determination of the stool acidity gives interesting data, but offers little from the standpoint of diagnosis, prognosis or treatment.

MCCLELLAND, Cleveland.

DRIED MILK FEVER. M. P. LEREBOULLET, Progrès méd, July 25, 1931, p 1333.

The author has frequently observed a temperature as high as 42 C. (107.6 F.) in infants fed dried milk. All of these infants were on rather concentrated formulas. The cause of this is not infection, intoxication or anaphylaxis, but simply an insufficiency of water in the infant's diet. Treatment is simply a reduction of the concentration.

SANFORD, Chicago.

RICKETS AND ANTIRACHITIC THERAPY. EMIL WIELAND, Schweiz. med. Wchnschr. **61**:25 (Jan. 10) 1931.

Professor Wieland presents an excellent clinical picture of rickets. He states that it is the most common disease of infancy. More than 80 per cent of all infants under 1 year show signs of florid rickets. Rickets rarely occurs during the second and third years. It is never congenital, but the disposition to rickets is probably inherited. Wieland believes that rickets always begins during extra-uterine life, but that it may begin very early in premature infants.

The discussion of the pathology and blood chemistry is in accordance with the standard teaching. Wieland emphasizes especially the nervous system involvement (sweating, hypotonus, etc.). He advises the use of quartz light therapy, and states that treatment must continue over a period of from four to six weeks. He states that sunlight is an excellent therapeutic measure, but that it is unstable and uncertain. He warns against overdosage of irradiated ergosterol.

KREITZ, Ann Arbor, Mich.

PROPHYLAXIS OF RICKETS. MARTINEZ VARGAS, Med. de los niños **32**:97 (April) 1931.

The use of irradiated ergosterol and its comparison with cod liver oil are discussed in relation to the prevention of rickets. The author stresses the use of farinaceous foods before the age of 6 months or before the eruption of teeth. Regular feeding intervals with food of good quality and well prepared, as well as scrupulous cleansing of the hands in older children before eating, are important.

DWYER, Kansas City, Mo.

GOUT IN AN INFANT FIVE WEEKS OLD. E. MAYER VON SCHOPF, Klin. Wchnschr. **9**:2148 (Nov. 15) 1930.

A case report is given with autopsy findings. Its importance in gout lies in the evidence that uric acid arises only from the endogenous purine metabolism, and the essential importance of constitutional and pathologic factors. Exogenous influences, such as diet, environment and mode of life, had evidently no effect. The reason for the retention of uric acid could not be determined. Histologically the bone showed no evidence of inflammation, but the kidney was contracted. A tremendous number of crystals were present in the interstitial tissues.

SILVERMAN, Syracuse, N. Y.

A NEW PRINCIPLE IN THE EVALUATION OF IRRADIATED ERGOSTEROL. JOSEF WARKANY, Klin. Wchnschr. **9**: 2152 (Nov. 15) 1930.

Within forty-eight hours it is possible to evaluate a preparation of irradiated ergosterol as to its antirachitic power. Rabbits kept on fresh greens excrete urine that is practically free from phosphates. After the ingestion of active irradiated ergosterol there is a marked increase in urinary phosphates. The Bell-Doisy-Briggs method of phosphate analysis was used after ashing the urine. While this is chiefly a qualitative method, it is simpler than the micromethod in serum.

SILVERMAN, Syracuse, N. Y.

TREATMENT AND PROPHYLAXIS OF RICKETS BY MEANS OF SMALL DOSES OF QUARTZ LAMP RADIATION. H. VOLLMER, Klin. Wchnschr. **9**:2300 (Dec. 6) 1930.

The author finds the results about the same whether large or small doses of ultraviolet rays are used in treatment. He rather feels that in many cases too large an amount is given, which wastes time and electric power. Forty-three infants were given weekly treatments of four or five minutes' duration on the chest and back at a distance of 80 cm. He considers this the minimal effective dose and believes that there is little difference in the results between minimal and larger doses.

SILVERMAN, Syracuse, N. Y.

EXPERIMENTAL RICKETS. T. SKAAR, Acta paediat. (supp. 1) **12**:1 (May 26) 1931.

The experiments were designed to show, in puppies, the effect of rickets and of various experimental procedures on the calcium, magnesium and phosphorus balance, on the serum calcium and phosphorus levels and on the inorganic composition of bone. The vitamin C content of the diet was varied. Animals lacking both vitamins C and D showed more marked chemical changes than those lacking vitamin D alone. Those lacking only vitamin C had a positive calcium balance at a lower level than the controls. Clinical scurvy in the dog has never been described, but the author cites the chemical evidence of his experiments to prove that the withholding of vitamin C produces a biochemical disturbance in these animals.

Some animals on a ricket-producing regimen were fed an excess of calcium lactate, others an excess of sodium phosphate and others a mixture of tricalcium phosphate and calcium carbonate. Calcium slows but does not check the development of rickets. Sodium phosphate aggravates the rickets, though it improves the phosphorus balance. Tricalcium phosphate acts much like calcium lactate. The magnesium balance is independent of both calcium and phosphorus in the diet.

The work is reported in great detail. It does not offer much that is essentially new except in so far as the studies are made on dogs rather than on rats. Students of the rickets problem, however, will find herein a wealth of fundamental data.

McINTOSH, New York.

STUDIES ON THE MINERAL METABOLISM DURING PREGNANCY AND LACTATION AND ITS BEARING ON THE DISPOSITION TO RICKETS AND DENTAL CARIES. K. UTHEIM TOVERUD and G. TOVERUD, Acta pædiat. (supp. 2) **12**:1 (May 28) 1931.

A negative calcium balance was found in twenty-one, and a negative phosphorus balance in twelve, of twenty-seven determinations on primiparae at various stages of pregnancy. The diet given was an average normal for Norwegian women, but showed itself lacking in minerals since the balance could be improved by the addition of milk or calcium lactate. Usually the addition of vitamin D failed to improve the mineral balance when the mineral intake was low. If the daily calcium and phosphorus intake was kept above 1.6 Gm., and the diet contained liberal amounts of cod liver oil, viosterol or eggs with fruits and vegetables (alkaline ash), the balance remained positive. Lactating women on the same diet often showed negative calcium and phosphorus balances, and the calcium content of their milk was below normal. This could be corrected by feeding calcium, but the milk remained low in phosphorus.

By feeding a dog a diet low in calcium, phosphorus and vitamins A and D throughout gestation, marked losses of calcium and phosphorus from the mother's body could be demonstrated. The serum calcium and phosphorus which had both fallen progressively during the pregnancy, fell off sharply after the birth of the puppies, so that on the eighth day of lactation the values were 5.2 and 2.9 mg. per hundred cubic centimeters, and tetany developed. None of the puppies showed

demonstrable rickets at birth, though the body as a whole, and the femur in particular, showed low mineral content in a killed control. If the mother's diet was deficient in calcium, phosphorus and vitamins A and D during gestation and lactation and the puppy's diet the same after weaning, growth was slow and rickets appeared early (at the age of 7 weeks). If the mother's diet was normal during gestation but deficient during lactation, growth was somewhat more rapid and the appearance of rickets delayed (at 11 weeks). When the mother's diet was normal throughout, but the puppy was weaned onto a deficient diet, growth was about normal and rickets did not appear until 13 weeks of age. Changes in the teeth—hypoplasia and deficient calcification—closely paralleled the dietary defects of the mothers.

Another bitch fed on a diet low in calcium and phosphorus but containing normal amounts of vitamins A and D showed even more marked negative balances during gestation, but the serum calcium and phosphorus remained more nearly at the normal level. Her puppies showed similar changes at birth to those of the other group, but as they grew up they showed osteoporosis rather than rickets. Magnesium balances showed no definite changes.

Several case histories of children with hypoplastic and carious teeth are analyzed in the light of the dietetic and hygienic deficiencies of the mother during pregnancy.

It is concluded that the prevention of rickets and dental caries, to be effectual, should start in fetal life.

McIntosh, New York.

The Distribution and Frequency of Rickets in One of the Fishery Districts of Finmark and the Relation of Diet to the Disorder. J. Kloster, Acta paediat. (supp. 3) **12**:1 (May 28) 1931.

A rickets survey at latitude 70 degrees north showed a general morbidity of 43 per cent in 376 infants and children (up to 7 years of age). Among infants rickets appeared most commonly in those not taken out-of-doors, in those born in the autumn, in those not breast-fed during the first four months of life and in those in whom the transition from a milk diet to a mixed diet was delayed.

McIntosh, New York.

Buttermilk in Infant Feeding. Cenek Saitz, Časop. lék. česk. **68**:733 (May 17); 778 (May 24) 1929.

The author reviews and discusses the literature on buttermilk and acid milk feeding since the work of Nils Rosen in 1793. Variations, such as albumin milk, flour mixtures, butter additions, dextrin, maltose and other sugars, are compared. The relative merits of breast milk are compared to those of buttermilk. Lactic acid (1) in small doses enhances the physiologic effect of food (large doses have the opposite effect), (2) activates ferments, (3) increases the activity of the pancreas, intestinal glands and bile, (4) has a beneficial effect on diastatic action, (5) hastens peptonizing, (6) has a beneficial effect on the nitrogen component exchange, (7) in various concentrations affects the exchange of all components, (8) hinders putrefaction, (9) regulates peristalsis, (10) is a factor in the absorption and retention of organic and inorganic components and (11) lessens the formation of soap stools. Marfan summarizes the advantages as a modification of protein, decrease in fat, reduction of lactose, smoothness due to the addition of a very little starch, and reduction of fermentation by lactic acid. Good results are cited in feeding premature and congenitally weak infants and in mixed feeding, rapid weaning, acute diseases, gastro-intestinal diseases, chronic nutritional diseases, rickets, anemia, syphilis and tuberculosis. Contraindications are the primary period of severe vomiting and diarrhea, overacid stools and constipation.

Stulik, Chicago.

Prenatal Conditions

A Unique Anomaly of the Biliary Tract: Communications Between Cystic and Hepatic Ducts with Occlusion of Common Duct and Separate Entrances Into the Duodenum. A. Gentile, Am. J. M. Sc. **182**:95 (July) 1931.

A case is reported in which there were communicating channels between the hepatic and cystic ducts, separate entrances of the common and hepatic ducts into the duodenum and complete occlusion of the common duct. This congenital anomaly resembles the normal anatomy in some birds, and in reptiles to some degree.

Embryologically, the liver primordium from the duodenum failed to elongate normally and the growing gut appropriated the undivided portion, thus making two separate entrances of the biliary ducts into the intestine. The liver bud began its growth, and, due to the close proximity of the cystic and hepatic ducts, connecting branches were formed from earlier duct evaginations.

Henske, Omaha.

Congenital Heart Disease: A Persistent Ostium Atrioventriculare Commune with Septal Defects in a Mongolian Idiot. G. M. Robson, Am. J. Path. **7**:229 (May) 1931.

A case of persistent ostium atrioventriculare commune with a defect in the base of the interventricular septum and a persistent ostium primum in a mongolian idiot dying of scarlet fever at 4 years and 9 months is reported. The child was cyanotic at birth and had recurrent attacks of cyanosis associated with pulmonary infections after 6 months of age. Death was sudden with extreme cyanosis during a mild attack of scarlet fever. The heart weighed 183 Gm.; the left ventricle was 14 mm. thick; the right ventricle 13 mm. thick; the aortic valve ring 4.5 cm. in circumference, and the pulmonary ring 5 cm. The aortic and pulmonary valves and all great vessels were normal. The ductus arteriosus and foramen ovale were closed. The mitral and tricuspid orifices were represented by a common orifice guarded by five valves. Both ovaries were devoid of follicles and germinal epithelium and composed of what were vestigial wolffin tubules. The author believes that the cardiac condition is due to a failure in the upward growth of the endocardial cushions and union with the septum primum. Four of nine similar cases reported in the literature occurred in mongolian idiots.

Moore, Cleveland.

Foetal Blood Studies: II. The Lactic Acid Content of Umbilical Cord Blood Under Various Conditions. N. J. Eastman and C. M. McLane, Bull. Johns Hopkins Hosp. **48**:261 (May) 1931.

The lactic acid content of maternal and umbilical blood was studied in twenty-four cases including seven of fetal asphyxia. The blood lactic acid of the fetus in utero is within normal limits. The fact that the arterial and venous bloods of the fetus in utero show no detectable differences in lactic acid content is taken to indicate that, normally, little of this acid is produced in fetal tissues. At birth, the lactic acid of infants is regularly elevated from 28 to 45 mg. per hundred cubic centimeters with an average of 35. There is no difference in the lactic acid content of the umbilical vein blood and umbilical artery blood. The increase is due to simple diffusion from the mother whose blood lactic acid is increased as the result of muscular activity incident to labor.

In asphyxia, there is a definite endogenous production of lactic acid, the levels rising above those in the maternal blood and reaching as high as 90 mg. per hundred cubic centimeters. It seems probable that asphyxia neonatorum is associated with considerable acidosis, but the authors draw no conclusions as to how important a factor it may be.

Lyttle, New York.

CONGENITAL LARYNGEAL STRIDOR DUE TO MICROMANDIBULAR DEVELOPMENT. HARRY P. GARFINKEL, Dental Cosmos **73**:600 (June) 1931.

The author briefly describes the condition of stridor, giving the etiology, anatomy of the part, physical signs, diagnosis and treatment. He cites a case from the pediatric service of the hospital with which he is affiliated. This case is due to a very much underdeveloped mandible, causing the tongue to be forced back into the pharynx, partially occluding the respiratory passages and thereby giving rise to stridor or the noisy form of breathing, particularly during inspiration. This condition, which occurs during early infancy, is associated with malnutrition and cyanosis, usually as a result of the deformity. It usually disappears during the second or third year. The treatment used consisted of an appliance suspended from a headgear with wire extending downward on both sides, exerting a forward pressure against the angles of the mandible, tongue and floor of the mouth and displacing these structures forward, thereby relieving the obstruction to normal respiration.

MARKUS, Philadelphia.

HYPERTELORISM. WILLIAM A. REILLY, J. A. M. A. **96**:1929 (June 6) 1931.

Hypertelorism, a term applied by Grieg to a developmental defect of the lesser wings of the sphenoid bone with early ossification and excessive growth, is probably more common than reports would indicate. The skull is brachycephalic and the eyes are widely separated. Mental retardation can occur, and in some cases the condition is familial. The author reports four cases, bringing the total to seventeen in the literature.

BONAR, Salt Lake City.

A NOTE ON CONGENITAL DEVELOPMENTAL DISEASES. F. PARKES WEBER, Brit. J. Child. Dis. **28**:34 (Jan.-March) 1931.

The author makes a plea for an "atlas" showing, by means of photographs, roentgenograms, sketches and diagrams, the macroscopic structural congenital developmental abnormalities, both external and internal.

LANGMANN, New York.

THE PERMEABILITY OF THE PLACENTA TO UROBILIN. M. ROYER, Compt. rend. Soc. de biol. **102**:421, 1929.

Urobilin in the livers of embryos was determined before and after the intravenous injection of urobilin into pregnant dogs. The considerable increase of urobilin in embryonic livers explains the constant presence of urobilin in the urine of the new-born infant.

KUGELMASS, New York.

ALKALINE LIME PHOSPHATES AND CARBONATES IN THE FETAL LIVER OF VERTEBRATES. G. ROUSSEL and DUFOUR-DEFLANDRE, Compt. rend. Soc. de biol. **106**:529 (Feb. 27) 1931.

Fetal calf and sheep livers of different ages were studied as to the presence of calcium phosphate and calcium carbonate. The usual chemical precipitation methods were used in order to produce calcium oxalate and ammonium phosphomolybdate, subsequently identified microscopically for crystallization type. The authors do not give any figures, but conclude that both of these salts are present in increasing quantities with the age of the fetuses studied.

WAHL, Cleveland.

PRESENCE OF POTASSIUM, SULPHUR, MAGNESIUM, MANGANESE, ARSENIC AND PHOSPHORUS IN FETAL LIVERS OF VERTEBRATES. S. ROUSSEL and DUFOUR-DEFLANDRE, Compt. rend. Soc. de biol. **106**:1118 (April 24) 1931.

Calf and sheep livers were studied and tests made for potassium, sulphur, magnesium, manganese, phosphorus and arsenic. In comparison with the abundance of phosphorus, the other elements were found only in small quantities.

WAHL, Cleveland.

THE COPPER CONTENT OF THE ORGANS OF THE FETUS. I. I. NITZESCU, Compt. rend. Soc. de biol. **106**:1176 (April 24) 1931.

Various tissues from sixteen human fetuses varying in age from 5 months' gestation to term, born of normal mothers, as well as like tissues from five adults dying accidentally, were studied for copper content. In the fetus, the quantity varied from 9.86 to 61.93 (average, 26.2) mg. per gram of liver, while in the adult the variation was from 1.31 to 9.8 (average, 4.5) mg. This is in accord with other investigators. The results obtained in the other tissues of the body did not warrant a definite opinion as to any variation in the copper content of the fetus and adult.

WAHL, Cleveland.

A NEW VARIETY OF DWARFISM. A. LERI, F. LAYANI and JACOB WEILL, Presse méd. **39**:262 (Feb. 21) 1931.

Under the name "dyschondrosteosis," two cases of an unusual variety of dwarfism are described. A marked shortening of the extremities is the only deformity; the head, trunk, hands and feet are essentially normal. The forearm is shortened to such a degree that it is shorter than the hand. Both bones of the forearm are greatly curved, the radius transversely and the ulna anteroposteriorly. The most striking roentgen observation is the almost complete absence of the head of the radius and the lower end of the ulna; these bones cease to form any part of their respective articulations. The tibia and fibula are shortened to a like degree, but the extremities of these bones are present. The humerus and femur are shortened, but not as markedly as the other bones, and their form is normal. There is no lordosis or isodactylism. This condition has little in common with the usual form of chondrodystrophy or achondroplasia. There is no evidence of rickets. A history of syphilis was obtained in the mother of one of the patients, but stigmas of congenital syphilis were entirely absent.

BIEKER, St. Petersburg, Fla.

STATISTICAL STUDIES OF PREMATURE INFANTS. SALVATORE RAPISARDI, Pediatria **39**:309 (March 15) 1931.

This paper represents a study of 133 premature infants encountered in 1,000 consecutive births at the Royal Obstetrical Clinic of Catania. Among the principal causes of prematurity the author found, in the order of their frequency: (1) diseases and anomalies of the pelvis and pelvic organs (premature detachment of the placenta, placenta praevia marginalis, placenta praevia centralis, pelvic deformities), (2) twin pregnancies, (3) syphilis and (4) cardiopathies. The mortality is influenced by the weight of the newly born infant, by the cause of prematurity and especially by the duration of intra-uterine life.

SIGNORELLI, New Orleans.

THE PROGNOSIS OF PREMATURE INFANTS. GERTRUD GRIES, Monatschr. f. Kinderh. **49**:441 (April) 1931.

The author reviews the material in the Cologne Children's Clinic during the years 1920 to 1929. The number of premature infants has increased. This is not due alone to the fact that the improved facilities attract more patients, but also to an actual increase in the number of premature births. In the 383 prematures studied, the mortality averaged 55.4 per cent. This high mortality was due particularly to infections, especially pneumonia, induced perhaps by the tube feeding. One-fourth of the deaths were due simply to "weakness," and one-fifth to cerebral hemorrhage. The mortality showed some relation to the body temperature on admission. A temperature below 34 C. (93.2 F.) on admission offers a very poor prognosis. The etiology of prematurity depends somewhat on the general health of the mother and anomalies in the course of the pregnancy, but in almost 60 per cent of the cases the cause was unknown. The condition of the premature

infants after discharge from the clinic was satisfactory. During the first year the children remained a little below the average physically, but soon made this up. Mentally they were normal.

GERSTLEY, Chicago.

A CASE OF PARTIAL GIGANTISM. IHSAN HILMI, Monatschr. f. Kinderh. **50**:29 (May) 1931.

The author reports the case of a 6 year old girl showing gigantism of the left leg; he includes photographs and roentgenograms. Of special interest in this case was the excessive growth of four toes, leaving the great toe normal.

GERSTLEY, Chicago.

BLOOD GROUPS IN OBSTETRICS AND GYNECOLOGY: II. BLOOD GROUPS OF IMMATURE HUMAN FETUSES. MAGOSHIRO OKU, Jap. J. Obst. & Gynec. **13**: 472 (Oct.) 1930.

The author has carefully examined the blood groups of 115 immature human fetuses, and has arrived at the following conclusions: 1. The isohemagglutinogen is found in the erythrocytes of immature fetuses as early as the second month of gestation. 2. It follows the laws of inheritance, the same as after birth. 3. The isohemagglutinogen has become definitive by the beginning of the third month of gestation and does not later change from one type to another. 4. The erythrocytes have the power of absorbing the corresponding isohemagglutinin the same as the corpuscles of the adult. 5. The agglutinability of the erythrocytes is weaker in the fetus than in adults. It increases as pregnancy advances. 6. Isohemagglutinin is present in the fetal serum as early as the fifth month. 7. This is not of fetal but of maternal derivation. 8. The relation of the agglutinogen and agglutinin is quite different in fetal and adult blood. There is no interaction in fetal blood. 9. The isohemagglutinin in the fetal serum is intimately related to the blood type of the mother as well as the fetus. 10. The isohemagglutinin in the serum of the fetus is of little value for determining the blood type of the fetus. 11. The determination of paternity by means of the fetal blood type is as feasible as in the infant, and is of definite value in forensic medicine.

ADAIR, Chicago.

BLOOD GROUPS IN OBSTETRICS AND GYNECOLOGY: III. GROUP SPECIFICITY OF VARIOUS ORGAN CELLS IN HUMAN FETUS. MAGOSHIRO OKU, Jap. J. Obst. & Gynec. **13**:524 (Oct.) 1930.

The author has studied the cells derived from the lung, liver, kidney and brain of fetuses from the second to the tenth month of gestation. 1. The cells of the lung, liver and kidney have group specificity corresponding to the blood group. This can be traced backward to the end of the third month. 2. It cannot be demonstrated earlier than the first half of the third gravid month. 3. No group specificity can be demonstrated in the brain cells at any period. 4. As the result of the present experiment, it has been learned that the blood type of the fetus, after the fourth month of pregnancy, can be ascertained by means of organ cells. This is of definite medicolegal value in cases in which the fetal blood is not obtainable.

ADAIR, Chicago.

Diseases of the New-Born

ERYTHROBLASTOSIS WITH JAUNDICE AND EDEMA IN THE NEWLY BORN. J. A. FERGUSON, Am. J. Path. **7**:277 (May) 1931.

Six cases are reported in which there was abnormal extramedullary hematopoietic activity with enlargement of the spleen and liver. Two cases showed edema and three jaundice. The relation of these to hydrops congenitus and icterus neonatorum is discussed. The author believes that this pathologic syndrome represents a definite disease entity and designates it erythroblastosis of the newly born.

MOORE, Cleveland.

STREPTOCOCCUS HEPATITIS. H. E. MACMAHON and F. B. MALLORY, Am. J Path. **7**:299 (May) 1931.

Two of the five cases of streptococcus hepatitis reported here occurred in infants In one, 8 days of age, the lesion was associated with an abscess of the wrist; the other occurred in a new-born infant associated with an extensive infratentorial hemorrhage. *Streptococcus haemolyticus* was isolated in both cases. The report of the cases is followed by the results of the experimental production of similar lesions in guinea-pigs and rabbits. The authors suggest a relation between streptococcus hepatitis and acute yellow atrophy and suggest full histologic and bacteriologic study of such cases.

MOORE, Cleveland.

THE ELASTIC LAYER IN THE CEREBRAL VESSELS: STUDIES OF THE NEW-BORN AND OF CHILDREN. C. R. TUTHI Arch. Neurol. & Psychiat. **26**:268 (Aug.) 1931.

The elastic layer of the cerebral blood vessels is not well developed at birth, small arterioles in the substance of the brain having few or no elastic fibers during the first year of life. This lack of development may account for the ease with which intracranial hemorrhages occur in new-born infants. In childhood, the elastic layer splits at the branching of the large and small vessels. This splitting sometimes surrounds the whole lumen of the vessel. At times these fibers undergo hyaline changes which cause the branch to appear as an aneurysm. Retrogressive changes of these areas sometimes occur during childhood, as is evidenced by calcification. Such changes were demonstrated in a child of 7 years with an abscess of four months' standing. Inflammation and intoxication may increase the splitting of these elastic fibers, leading to meningitis or other pathologic conditions.

BEVERLY, Chicago.

NEONATAL CARE. JOHN D. VAN CLEVE, M. J. & Rec. **134**:30 (July 1) 1931.

The care of the newly born infant has come into its own only in very recent years. It is that period of life which is most neglected. The author discusses: (1) respiration in the newly born infant, (2) the care of the cord, (3) the temperature maintenance, (4) the newly born infant's clothing, (5) common cause of death, (6) malformations and (7) feeding and habit spasm. The article is accompanied by a record card which the author suggests for the routine examination of the new-born infant.

WILLIAMSON, New Orleans.

OTITIS MEDIA WITH PURULENT MENINGITIS IN AN INFANT NINE DAYS OLD. GLADYS H. DODDS, Arch. Dis. Childhood **6**:71 (Feb.) 1931.

This is a case report of primary otitis media with purulent meningitis in a baby 9 days old. The infant was sick for four days before it died. The meninges were congested, and there was considerable greenish pus on all surfaces of the brain, being more marked around the base. The right ear showed no abnormality. The left ear and surrounding bone were soft and filled with greenish pus. The causal organism could not be isolated.

KELLY, Milwaukee.

CONGENITAL HYDRONEPHROSIS. LACOMME and FAYOT, Nourrisson **19**:187 (May) 1931.

In an infant who died at the age of 5 days after hematemesis and melena, autopsy revealed a hydronephrotic kidney on the left side. It was the size of a hen's egg. The wall was quite thin and contained renal tissue; the central cavity

contained urine. The lumen of the ureter showed obliteration of its lumen about 0.5 cm. from its renal attachment. There were also two renal arteries but only a single vein.

McCLELLAND, Cleveland.

THE REFLEXES IN THE NORMAL NEW-BORN. FRANCESCO ROLANDO, Pediatria **39**:645 (June 15) 1931.

This study was made with the view of establishing the response of the various reflexes in normal new-born infants. Eighty infants who appeared clinically free from all abnormalities were systematically examined during the first week of life, and the detailed results systematically tabulated. From this detailed study it appears conclusive that the several reflexes in the new-born present so wide a variation in their reactions that it is difficult to systematize their clinical or pathognomonic significance as in the adult. These conclusions, of course, do not apply to cases in which marked inequalities exist in the reaction obtained on one side of the body from that obtained on the other; nor in cases in which there exist wide discrepancies from the normal, especially when marked by an absence of reaction.

SIGNORELLI, New Orleans.

THE CONTENT OF DIPHTHERIA ANTITOXIN IN THE BLOOD OF NORMAL NEW-BORN INFANTS AND OF NEW-BORN INFANTS WHOSE MOTHERS RECEIVED ANTITOXIN TREATMENT DURING PREGNANCY. C. SORRENTINO, Pediatria **39**:849 (Aug. 15) 1931.

Using Roemer's method, the author has estimated the content of diphtheritic antitoxin in the blood of eighteen normal new-born infants ranging in age from 40 days to 4 months, and of fourteen new-born infants whose mothers had received graded doses of antidiphtheritic (Ramon's) serum from the seventh month to the end of gestation. The results of his studies are tabulated as follows: 1. In the majority of cases the infant possesses a notable content of diphtheritic antitoxin in the blood when it is born. 2. The transmission of antitoxin is effected from the mother to the fetus through the placental circulation. 3. There is a direct parallelism in the antitoxin content of maternal and neonatal blood. 4. It is possible to vaccinate the infant successfully before birth by means of administering antitoxin to the mother during the late months of pregnancy.

SIGNORELLI, New Orleans.

A RARE CASE OF DRY GANGRENE OF THE RIGHT FOREARM IN A BABY TEN DAYS OLD. A. GRASSI, Riv. di clin. pediat. **29**:120 (Feb.) 1931.

A baby was born with the cord wound twice around the neck; marked cyanosis was present, which soon disappeared except in the right forearm. When first seen by a physician, the child was 10 days old. Gangrene was present. The arm was wrapped in alcohol for sixteen days, and then amputation was done below the elbow, as there was a definite line of demarcation. The child recovered.

The author discusses the possible cause of gangrene of the forearm in the new-born. In this instance, he believes that the cause was thrombosis due to pressure of the arm between the pelvis and the fetal head during labor.

HIGGINS, Boston.

THE INFLUENCE OF SOME FACTORS ON THE WEIGHT OF NEW-BORN BABIES. A. O. GERSCHENSON, Ztschr. f. Kinderh. **51**:20 (May) 1931.

In the hunger years (1921 and 1922) the percentage of babies with a low weight, from 2,500 to 3,000 Gm., was almost twice as great as in more prosperous years. The number of babies of medium weight, from 3,000 to 3,500 Gm., remained almost unchanged. This diminution was about twice as great for multiparae as

for primiparae. Therefore, when food is scarce, pregnant women should be given rations, especially if they are multiparae. There is a connection, unquestionably, between the weight of the baby and the time of the year in which it is born, which is apparently to be explained by an increase in metabolism in the mother, due to the action of the rays of the sun and, consequently, to better nutrition of the fetus. The weight of the baby is influenced also by the age of the mother, the smallest percentage of babies with a low weight being born to mothers aged from 25 to 35 years. The interval between pregnancies also has an influence, from three to five years being the most favorable interval. Propaganda would seem to be necessary by means of clinics to rationalize the culture of babies.

EMERSON, Boston.

ICTERUS NEONATORUM GRAVIS. MACCLURE, Ztschr. f. Kinderh. **51**:86 (May) 1931.

A baby, 3 days old, which might have been premature, was admitted because of icterus and fever, having had marked jaundice at birth and enlargement of the liver and spleen. She had mild convulsions on the fourth and fifth days, occasional vomiting and an increase of the jaundice in the third week, and she died on the eighteenth day. Pustules appeared on the skin before death. The stool contained bile. The red blood cell count was 2,480,000; the hemoglobin content 75 per cent, and the resistance to salt solution normal. It was impossible to group this case according to Kleinschmidt's scheme for icterus neonatorum gravis, premature, septic or familial, since, on the one hand, jaundice present at birth, enlargement of the liver and spleen, bilirubinuria, anemia, a positive van den Bergh test and cerebral irritation spoke for the familial type, while, on the other hand, the absence of erythroblastosis, and an irrelevant family history spoke against it.

Blood destruction lies at the bottom of this case; the cause is obscure, but the evidence is extensive: erythrophagia, erythrocytorrhexis, erythrolysis in the liver, the breaking down of hemoglobin into iron and biliary pigment and great siderosis in the spleen and liver. In agreement with Schminke, the author looks on this case as a retention icterus because of injury to the excretory functions of the hepatic cells. The bile excreted into the bile ducts possessed an increased capacity for coagulation, perhaps because of admixture with protein substances, so that the bile passages were blocked, which resulted in the absorption of bile.

EMERSON, Boston.

BIRTH INJURIES IN THE NEW-BORN: VI. EXPERIMENTAL INVESTIGATION OF THE MECHANICAL PROCESS OF INTRACRANIAL HEMORRHAGE IN THE NEW BORN. HIDEO YAGI, Jap. J. Obst. & Gynec. **13**:551 (Oct.) 1930.

Yagi has made some investigations on rabbits and human fetuses, and believes that stasis, pressure and resistance are the three important factors in the production of intracranial injuries. Some investigations on the pregnant uterus, by means of his rabbit tocodynamometer, indicates that pressure plus stasis is of great importance. He further experimented with some dead human fetuses of 9 and 10 months' gestation and found that pressure and weight, continuous and sudden, produced injury. It is also his opinion that the direction of the pressure is important. In a study of the intracranial vessels, especially the vein of Galen, by microscopic methods, he showed a dearth of elastic fibers with thinner vessel walls in younger fetuses.

In conclusion, he believes that the resistance of the intracranial tissues, especially of the vessel walls, as well as the strength of the cranial bones, is important. The various types of subdural, leptomeningeal, ventricular and intracerebral hemorrhages are caused by the three factors already mentioned. They differ in each clinical case and need to be evaluated.

There is no labor without pressure, and stasis occurs especially in the second stage. Often they are parallel and proportional, but sometimes one or the other becomes excessive. The resistance also varies. All of these different factors should be understood as of the very greatest importance in causing intracranial injuries to the fetus during birth.

ADAIR, Chicago.

THE NEW-BORN PERIOD. L. LEMEZ, Časop. lék. česk. **68**:951 (June 28) 1929.

The author reviews the literature showing that there is a difference in the reaction of the new-born infant to various stimuli in contrast to the reaction of the older person. This has been called "allergy of the new-born" by several authors. According to Becker there is a lack of local reaction to antigens found in the older organism. With some antigens, such as foreign blood proteins, there may be neither a local nor a general reaction. This is further illustrated in the reaction in erysipelas, staphylococcus infection, vaccination, meningitis — which may manifest itself as merely a debility — and pneumonia. In the premature infant there seems to be a definitely decreased leukocytic action and an increase in the tendency toward a hemorrhagic diathesis.

STULIK, Chicago.

A CASE OF MORBUS RITTER (DERMATITIS EXFOLIATIVA NEONATORUM). N. C. VAN VONNO, Nederl. tijdschr. v. geneesk. **75**:1932 (April 11) 1931.

A bacteriologic and histologic investigation was made in a typical case of dermatitis exfoliativa. The bacteriologic examination of the sterile prepared corium demonstrated numerous colonies of Staphylococcus albus and some of Staphylococcus pyogenes and aureus. From the blood Staphylococcus pyogenes-albus could be cultivated. Histologic examination of the skin showed that it was universally affected. The subepithelial tissue was degenerated; the epithelium itself was partly excoriated in an irregular way. There was a strong "Quellung" of the skin.

The author concludes that dermatitis exfoliativa is not a reaction but an infection of the skin with Staphylococcus pyogenes-albus, which results in a disease of the whole organism.

VAN CREVELD, Amsterdam, Holland.

Acute Infections

NONSUPPURATIVE ENCEPHALOMYELITIS ACCOMPANYING CHICKENPOX. H. M. ZIMMERMAN and HERMAN YANNET, Arch. Neurol. & Psychiat. **26**:322 (Aug.) 1931.

A 13 months old child developed convulsions three days following the onset of chickenpox. Death occurred twenty-four hours later. Autopsy limited to the brain and cord revealed a widespread noncharacteristic degenerative lesion of the ganglion cells, together with a perivascular destruction of the myelin sheaths in the white matter of the parietal and occipital lobes. There was an extensive phagocytosis of fat in these regions, and collections of fat granules were seen in the leptomeninges.

BEVERLY, Chicago.

THE RESULTS OF THE FIVE-YEAR TOXIN ANTITOXIN CAMPAIGN. Health News (New York State Dept. Health) **8**:29 (Feb. 23) 1931.

There were 23,326 fewer cases of diphtheria and 1,484 fewer deaths between 1926 and 1930 than in the five year period (from 1921 to 1925) preceding the toxin-antitoxin campaign. Thirty-five per cent of the children under 5 years of age must be protected against diphtheria before a community is safe from an epidemic. No city over 100,000 reached this goal, although Utica had a record

of 30 per cent; 32, 35 and even 38 per cent were reached in cities having from 50,000 to 100,000 population. The per cent protected in smaller cities was much higher.

AIKMAN, Rochester, N. Y.

TULAREMIA IN NORWAY. T. THJØTTA, J. Infect. Dis. **49**:99 (Aug.) 1931.

The author concludes that tularemia is not a rare disease in Norway since he was able to show that it was present nearly everywhere in that country. All the usual clinical types except the typhoidal have been seen. He thinks that the lemming may be a carrier there.

TOOMEY, Cleveland.

STREPTOCOCCI ASSOCIATED WITH EPIDEMIC SEPTIC SORE THROAT; THEIR RELATIONSHIP TO STREPTOCOCCI ASSOCIATED WITH SCARLET FEVER. MARY W. WHEELER, J. Prev. Med. **5**:181 (May) 1931.

Epidemics of septic sore throat occurred in Millbrook, Kingston and Clyde, N. Y., in 1930. These were studied bacteriologically and serologically together with similar studies in typical cases of scarlet fever occurring in the immediate vicinity.

The author concludes that the results obtained "illustrate that it is impossible by the methods now available to separate the streptococci associated with the epidemic septic sore throat and scarlet fever into definite groups which bear a specific relation to the particular type of infection induced."

TURNER, Chicago.

STUDIES IN THE BACTERIOLOGY OF EPIDEMIC INFLUENZA. PETER K. OLITSKY, Medicine **9**:387 (Sept.) 1930.

The author reviews all the work that has been done on this subject to date. He gives the outline of his technic and his findings. He concludes: "At the present time questions cannot be definitely answered." There are a number of factors that cause confusion. First, perhaps, is the difficulty of distinguishing between primary uncomplicated infection and secondary infection, particularly in pneumonias that develop in lungs that were previously injured by true etiologic agents. A number of organisms have been found by different observers, many of which are apparently due to secondary infection. One of the difficulties arising in this study is the inability to observe a patient in the early hours of infection. The bacteriologist, as a rule, sees the case only when secondary invasion by other than the specific etiologic organisms has taken place. Since an epidemic of influenza is usually of a fulminating type, it is difficult to study control cases. This has special reference to the serious difficulty of studying filter-passing anaerobes. Animal experiments are very unsatisfactory, since it is doubtful whether, in the animals usually used for this purpose, influenza as affecting the human organism actually occurs as a primary infection. Progress, however, has been made, since the largely important group of hemophilic bacteria, many of which are disease-producing, has been discovered as has the group of anaerobic filter-passing bacteria of the nasopharynx. It is hoped that through the employment of anthropoids rather than the ordinary laboratory animals some light will soon come from out the present chaos. The author concludes that the time is not far distant when exact knowledge of the etiologic agent of epidemic influenza will be obtained.

ROYSTER, University, Va..

ENDEMIC PURPURIC MENINGOCOCCUS BACTEREMIA IN EARLY LIFE: THE DIAGNOSTIC VALUE OF SMEARS FROM THE PURPURIC LESIONS. STAFFORD MCLEAN, New York State J. Med. **31**:684 (June 1) 1931.

Purpuric eruptions were present in 11 per cent of patients with meningococcal infections admitted to the Babies' Hospital. In seventeen cases the hemor-

rhagic lesions were examined for organisms, the results being positive in twelve. The author considers this method an aid to early diagnosis. The eruptive cases of meningococcus bacteremia are more apt to be of the fulminating type than are the more common examples of meningitis.

The report of the author's study of this subject is given in more detail in another publication.

AIKMAN, Rochester, N. Y.

VACCINIA OF THE FACE. LESLIE L. NUNN, Northwest Med. **30**:194 (April) 1931.

Nunn reports a case of vaccinia of the face acquired by a patient in sleeping with a recently vaccinated brother. He recovered showing four small round scars.

SCOTT, Philadelphia.

INTRADERMAL VACCINATION. MORRIS L. BRIDGEMAN, Northwest Med. **30**:231 (May) 1931.

Bridgeman has performed 535 vaccinations by the intradermal method with but 20 failures. He withdraws the vaccine from its capillary tube with a syringe, adds a few drops of saline solution and injects 0.1 cc. Usually four vaccinations can be done from one tube. There were no secondary infections and no large or unsightly scars. Many of these vaccinations were performed in the axilla; the exact site was not stated.

SCOTT, Philadelphia.

DISTRIBUTION OF DIPHTHERIA BACTERIOPHAGE. G. H. SMITH and ELIZABETH F. JORDAN, Yale J. Biol. & Med. **3**:423, 1931.

Phage for Bacillus diphtheriae has been obtained from sewage; from the throat washings, stools and urine of patients with diphtheria (in one instance ten days after the organism had disappeared from the throat); from carriers; from the throats of persons who were not carriers, or from whom the so-called diphtheroid forms could not be recovered by ordinary cultural methods; from the air and from the floor sweepings of laboratories in which work with diphtheria bacteriophage was being conducted, and from 100 per cent of all field cultures of diphtheria bacilli subjected to examination. The significance of this wide dissemination of diphtheria bacteriophage cannot be determined. Whether or not it represents an exceptionally delicate index of contamination pointing to a wider distribution of diphtheria bacilli or of forms allied to them remains unsolved. The relationship, if any exists, between diphtheria bacteriophage and diphtheritic infection is likewise unknown. Possibly some of the conflicting reports of the spontaneous appearance of bacteriophage may be explained by the demonstration that the bacteriophage corpuscle or the lytic principle adherent to particulate matter may be recovered from the air and from dust.

[ARCH. PATH.]

PNEUMONIA IN MEASLES. J. B. ELLISON, Arch. Dis. Childhood **6**:37 (Feb.) 1931.

In seventy-five cases of pneumonia complicating measles, cultures were taken directly from the lung. Micro-organisms of the influenza group were demonstrated in 46 per cent. Bacillus influenzae was obtained in pure culture in 31 per cent. In six cases Pneumococcus and B. influenzae were associated. B. influenzae and the hemolytic streptococcus were associated in five cases, which were fatal. Pneumococcus was found alone in twenty-one cases. The clinical features and leukocyte counts are given.

An examination of the lungs in eight fatal cases, in which B. influenzae was the predominating organism, revealed a characteristic interstitial pneumonia. From the standpoint of bacteriology, the prognosis is better in those cases that are due to Pneumococcus alone. The hemolytic streptococcus alone or associated with B. influenzae is far more dangerous.

KELLY, Milwaukee.

ACUTE EDEMA OF THE LUNGS IN MEASLES. P. NOBÉCOURT and J. LEREBOULLET, Arch. de méd d. enf. **34**:461 (Aug.) 1931.

Among the graver complications of measles, the various forms of bronchopneumonia, especially those associated with extreme cyanosis, may be considered the most important. A much rarer complication, however, is acute edema of the lung, first described by Legendre in 1837 and amplified by Rilliet and Barthez in 1843. The authors describe four cases in children, all developing suddenly in the course of measles. The dominating symptom was dyspnea, the patients soon developing orthopnea, with a respiratory rate as high as 60 and marked activity of all the accessory muscles. There was cyanosis, first of the face but soon extending over the entire body; hyperpyrexia accompanied this picture. The exact pathogenesis of these crises is unknown. In treatment, wet cupping is practiced over the thorax and loins; mustard baths are given and frequently repeated, and ouabain, in doses from 0.12 to 0.25 mg., is injected intravenously daily. Digitalis and camphor are also recommended for subcutaneous administration. Much dependency is placed on oxygen therapy. It is offered not only by inhalation, but subcutaneously.

AMESSE, Denver.

INCUBATION PERIOD OF MEASLES. P. LEREBOULLET and P. BAIZE, Arch. de méd d. enf. **34**:475 (Aug.) 1931.

Although most clinical observers declare that the incubation period of measles is free from disease phenomena, it is recognized that in certain instances one may discover such prodromal symptoms as slight fever, lassitude, anorexia, occasional vomiting, dry cough, mild coryza, diarrhea, cervical adenopathy, transient injection of the pharynx, loss of weight, eruptions and polymorphonuclear leukocytosis. Any of these may serve to put the attending physician on guard, when exposure to measles is suspected, and permit him to practice isolation promptly.

The authors were able to follow the clinical history of twenty-nine children from the moment of contact to the hour of onset; studies of the blood, of the weight curve and of the temperature changes were carried out in elaborate detail. In eighteen, or 62 per cent, definite manifestations of the approaching storm were noted; in eleven, or 38 per cent, the incubation period was wholly uneventful. This period, from the moment of contact to the first sign of oculonasal catarrh, varied from nine to eleven days; from the time of exposure, however, to the appearance of the eruption it was exactly fourteen days in every observation. When convalescent serum was given, the former period was increased to thirteen days. Various writers, among them Labbée, Rehn and Wunderlich, declare that there is a rise of temperature of about 1 degree in nearly every case, particularly toward the sixth or seventh day. In the series described, this elevation occurred in eleven of the twenty-nine cases. Meunier, in 1898, called attention to the consistent loss of weight during incubation of measles: in forty-three of forty-five cases this symptom was confirmed. Stimson has stressed this point recently, but the authors found only three of their patients losing weight. So far as the neutrophilic polynucleosis found by Combe in the premeasles stages, which gives way to mononuclear leukopenia with the onset of the eruption, only twelve cases could be satisfactorily studied and all of these exhibited changes of this kind in the blood.

AMESSE, Denver.

ANTIDIPHTHERITIC VACCINATION. D. DOPTER, Paris méd. **2**:91 (July 25) 1931.

The commission appointed by the League of Nations on diphtheria prevention reports as follows: The vaccine of choice is anatoxin given in three injections, at intervals of three weeks between the first and second injections, and two weeks between the second and third. These should be given subcutaneously. The ideal time of vaccination is at the end of the first year, and is necessary during the

preschool period. Intense propaganda should be carried out to acquaint the public with the necessity and harmlessness of antidiphtheritic vaccination.

SANFORD, Chicago.

STATISTICAL OBSERVATIONS IN SCARLET FEVER. G. PULIAREVITSCH, Schweiz. med. Wchnschr. **61**:81 (Jan. 24) 1931.

The author presents a series of statistics covering cases of scarlet fever in the Basal City Hospital from 1901 to 1905 and from 1923 to 1927.

The incubation period in 92 cases was: from one to three days in 36 cases (39 per cent); from four to six days in 29 cases (31.6 per cent); from seven to nine days in 17 cases (18.5 per cent), and from ten to twelve days in 6 cases (6.5 per cent). The incubation period was from one to six days in 70.6 per cent of the cases.

The complications were as follows: In 430 cases observed from 1901 to 1905, 136 patients had complications (34 per cent); 28.1 per cent had cardiac complications and 27.4 per cent kidney complications. In 401 cases recorded between 1923 and 1927, 95 patients had complications (24 per cent); 24.2 per cent had otitis media and 22.1 per cent kidney complications.

Urinalysis in 401 cases from 1923 to 1927 gave the following results: diazo reaction + in 21 cases (5.25 per cent), urobilin + in 105 cases (26.25 per cent) and urobilinogen + in 99 cases (24.75 per cent).

KREITZ, Ann Arbor, Mich.

SCARLET FEVER. RUDOLF MASSINI, Schweiz. med. Wchnschr. **61**:121 (Feb. 7) 1931.

Professor Massini presents an excellent discussion and review of over 4,000 cases of scarlet fever in Basel between the years 1900 and 1928. The discussion is more or less didactic, and his summary includes the following points: 1. Scarlet fever is a relatively harmless specific disease similar in many respects to dengue. 2. Streptococci are not the specific etiologic organisms. 3. Other organisms described as etiologic factors have not been sufficiently investigated. 4. A satisfactory laboratory method for diagnosing scarlet fever does not exist (agglutination, complement-fixation tests, etc.). 5. Scarlet fever has a characteristic syndrome, usually with a typical exanthem. It is more like dengue than measles. 6. Scarlet fever is often complicated by streptococcic infections and tuberculosis. 7. The heart is often primarily damaged. 8. Scarlet fever produces an immunity that is less than that of measles. 9. The period of infectiousness in most cases does not last over five weeks.

KREITZ, Ann Arbor, Mich.

COMPARATIVE STUDY OF THE ANTIGENIC VALUE OF SOME ANTIDIPHTHERITIC VACCINES. C. ARTUSI and V. MIGLIORI, Riv. di clin. pediat. **29**:295, 1931.

Three hundred and five children between the ages of 1 and 11 years were treated with one of three different methods of producing immunity to diphtheria. The Schick test furnished the control of their efficacy. The methods used were: (1) anatoxin (toxoid), (2) toxin-antitoxin and (3) the inunction method of Löwenstein. There were several procedures and preparations used in the anatoxin treatments; three or four subcutaneous injections at varying intervals were given; one procedure proved as efficacious as another. In the toxin-antitoxin treatment, two injections with a four week interval were given. Löwenstein's ointment was prepared in Vienna from a culture (nonfiltered) of diphtheria bacilli detoxified with formaldehyde. The percentage of negative Schick tests was as follows:

Method	No. Children	After 4 Weeks, per Cent	After 7 Weeks, per Cent	After 4 Months, per Cent
Toxoid	187	75	84	93
Toxin-antitoxin	61	10	38	63
Löwenstein	57	14	23	32

HIGGINS, Boston.

CASES OF CEPHALIC TETANUS IN CHILDREN. B. TRAMBUSTI, Riv. di clin. pediat. **29**:487, 1931.

Cephalic tetanus, or tetanus of Rose, is characterized by a triad of symptoms: trismus, spasm of deglutition and paralysis of the seventh nerve on the side of the lesion. The author reports eight cases in patients recovering from tetanus from wounds of the head. These represented one third of all the cases in children recovering from tetanus in the clinic at Florence. Six of the eight showed seventh nerve paralysis. As the paralysis is always on the same side as the wound, it seems that the facial nerve must be directly affected by the toxin produced near it.

HIGGINS, Boston.

THE FREQUENCY OF PARALYSIS OF THE SOFT PALATE IN MEASLES. D. CORDA, Riv. di clin. pediat. **29**:506 (June) 1931.

Of 195 patients who had recently had measles, 21 (10.8 per cent) were affected by paralysis of the soft palate to a greater or less degree for some period of time. In no case was there a positive culture for diphtheria bacilli from the throat. In a few cases, electrical reactions (galvanic current) were determined over the facial and median nerves; a hyperexcitability was found. Aphonia and regurgitation through the nose were occasionally observed. The author believes that his findings are due to a neuritis caused by a specific measles toxin.

HIGGINS, Boston.

ENCEPHALOMYELITIS AND VACCINATION. G. FIORE, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 652.

The author reports five cases of encephalomyelitis occurring eight, ten, ten, fourteen and twenty days following vaccination. All the patients recovered completely. He also reports a case of encephalitis, but not the postvaccinal type, occurring on approximately the same date as one of his other cases. He is of the opinion that the encephalitis is due not to the vaccinal virus, but to other neurotrophic viruses that happen to be in the community or in the vaccinated patient himself.

Vaccination against smallpox should not be done at a time when cases of encephalomyelitis are prevalent.

HIGGINS, Boston.

A CASE OF POSTSCARLATINAL NEPHRITIS WITH EDEMA OF THE LUNG. J. A. FALCONI, An. Soc. med. Quir. del Guayas Equidore **11**:79 (June) 1931.

A girl, aged 14 years, developed a moderate case of scarlet fever. The highest temperature was 40.5 C. (104.9 F.). Twenty-five cubic centimeters of scarlet-streptococcic serum (Lucius Hoest) was given. Two weeks later the child suddenly died of pulmonary edema. There had only been slight symptoms of a postscarlatinal nephritis, but the author believes that this was the cause.

SANFORD, Chicago.

ANTIVARIOLAR VACCINATION IN THE TREATMENT FOR PERTUSSIS. G. A. SCHIAVONE, Arch. argent. de pediat. **1**:593 (Dec.) 1930.

The author has made a study of the effect of smallpox vaccination on pertussis. The experiments were done on children in fairly good condition who had never been vaccinated against smallpox. The author concludes: 1. In a significantly large number of cases the pertussis disappeared soon or shortly after the vaccination became positive. 2. The author recommends this treatment for patients who are in fairly good condition and who have not been vaccinated previously. Similar experiments on children who have not been vaccinated previously have not been attempted.

The author refers to an article by M. E. Erlich (*Arch. de méd. d. enf.* **32**:666 [Nov.] 1929) who has studied the influence of other infections and smallpox vaccination on pertussis.

SCHLUTZ, Chicago.

A CLINICAL STUDY OF DIPHTHERIA OF EARLY INFANCY. PEDRO DE ELIZALDE, Arch. argent. de pediat. **2**:1 (Jan.) 1931.

The author classified diphtheria of the infant in three main groups: (1) true diphtheria, (2) local diphtheria and (3) diphtheria of the bacillary form, or the diphtheria carrier. The first group includes those forms of diphtheria that are characterized by a marked systemic intoxication. There is a form of the disease under this heading that the author calls "occult diphtheria," a form that he considers to be especially common in the infant. It is characterized by the presence of a severe general reaction and a very mild, or even the entire absence of, a local reaction. This form can frequently be diagnosed only by a knowledge of contagion.

In the second group he includes all the forms of the disease in which a local reaction alone is present. The nasopharynx and the skin are the most common sites, according to the author. He considers this to be the most frequent form of diphtheria in infancy. He further states that immunity to diphtheria may be local and general and while the infant in most cases possesses a passive general immunity from the mother, it does not, as a rule, possess a local immunity, a fact that would explain the relative frequency of the local form in infancy.

The author also points out that even a nonspecific serum may have a beneficial effect on the local lesions of diphtheria. On the other hand, there are forms of the disease that are resistant to the specific serum, regardless of the quantity administered.

The author recommends Lereboullet's treatment of the diphtheria carriers which consists in the instillation of an aqueous solution of merbaphen in each nostril three times a day (0.15 in 2 cc.). A disinfection of the nasopharynx can then be obtained in from three to five days.

SCHLUTZ, Chicago.

THE BACTERIOLOGY OF DIPHTHERIA. M. J. VERGNOLLE, Arch. argent. de pediat. **2**:23 (Jan.) 1931.

The author presents a general discussion of the bacteriology and immunology of diphtheria. In a study of 330 diphtheritic exudates, the following organisms were found associated with Klebs-Loeffler's bacillus: cocci and diplococci, 178; Diplococcus catarrhalis, 62; Diplococcus pneumoniae, 41; streptococci, 8; Bacillus fusiformis, 6; spirilla, 22, and fungi, 12. He concludes that the virulence of the diphtheria bacillus cannot be determined.

SCHLUTZ, Chicago.

MEDIASTINAL PLEURISY IN A SEVEN MONTHS OLD INFANT. P. DE ELISALDE and P. R. CERVINI, Rev. de especialid. **6**:7 (May) 1931.

A dystrophic child aged 6 months developed otitis media and infection of the upper respiratory tract. This was followed by pyelitis and bronchopneumonia. Roentgenograms were negative. Autopsy revealed a mediastinal pleurisy.

SANFORD, Chicago.

A CASE OF PSEUDOMEMBRANOUS BRONCHITIS WITH DIPHTHERITIC ANGINA. M. J. DEL CARRIL, Rev. de especialid. **6**:19 (June) 1931.

A child had a temperature of 39 C. (102.2 F.), a pulse rate of 120 and a typical diphtheritic membrane. The dyspnea present was expiratory, like an asthma, and there were sibilant râles all over the lungs. Thirty thousand units of antitoxin and oxygen inhalations were given. Later intubation was done, but the child died. Autopsy confirmed the clinical diagnosis.

SANFORD, Chicago.

ACUTE RHEUMATIC POLYARTHRITIS AND FOCAL INFECTION. G. VON CONTA, Klin. Wchnschr. **9**: 2140 (Nov. 15) 1930.

This article is based on 204 cases of typical acute rheumatic polyarthritis which were followed up after from five to eighteen years. In 113 there were chronic or repeated attacks of angina, in 9 there was infection of the teeth, and in 10 others polyarthritis followed acute infection. In 70 cases no other illness preceded the attack. In 74, rheumatic heart disease was definitely established. In those without heart involvement, recurrences were observed in 8 per cent. In those with heart involvement in the first attack recurrences were observed in 27 per cent. Operations for focal infections appear to make no difference in the number of recurrences. The author feels that constitutional and allergic factors are more important than infection.

SILVERMAN, Syracuse, N. Y.

UREMIA IN SCARLATINAL NEPHRITIS. A. ALTMANN, Klin. Wchnschr. **9**:2252 (Nov. 29) 1930.

Scarlet fever in the past five years has been mild, the mortality being 1.4 per cent. The complications have also been light. Nephritis, however, has shown an increase in incidence and severity in the last seven months. From Jan. 1, 1925, to Aug. 31, 1929, 3,089 patients with scarlet fever were admitted and of these, 45 died; 89 of the patients (2.9 per cent) developed nephritis; 21 of these came in with the complication and 68 developed it in the hospital.

Of the 349 admitted from Sept. 1, 1929, to March 31, 1930, 11 (3.1 per cent) died, and 24 (69 per cent) developed nephritis; of these, 9 came in with the complication and 15 developed it in the hospital. In the entire series of 113 cases, 20 patients or 18 per cent developed uremia. Of the 20 cases of uremia, 12 occurred in the first period and 8 in the last seven months. Sixty-five per cent of the cases of uremia showed a high nonprotein nitrogen content. This combined with a high blood pressure (over 130) is a serious sign, for, whereas more than half of the patients with nephritis became uremic, only one fourth of all the uremic patients had both of these signs. The amount of diuresis did not seem to bear a direct relation to the severity of the cases although half of the uremic cases showed a decrease to less than 100 cc. of urine daily. Hematuria and albuminuria seem without prognostic significance in uremia. Continued high fever in the absence of other complications after nephritis develops appears to be a serious sign. Somnolence, vomiting, headache and increased reflexes indicate a preuremic state, but by this time uremia cannot be prevented.

The rise of nonprotein nitrogen cannot be used as a basis for separating the various forms of uremia.

SILVERMAN, Syracuse, N. Y.

ADVACCINE (ANTIDENATURED VACCINE). L. A. SILBER and E. I. WOSTRUCHOWA, Ztschr. f. Immunitätsforsch. u. exper. Therap. **70**: 239, 1931.

The previous communication dealt with the use of glycerin as an antidenaturing menstruum for the vaccine. Owing to its locally irritating qualities, it was successfully replaced by saccharose and table sugar. (Fructose proved unsatisfactory.) The thermal death points of Bacterium paratyphosum B, of Bacterium abortum equi and of other bacteria suspended in the sugars mentioned were raised. Mice immunized with vaccines of Bacterium paratyphosum B and Bacterium abortum equi, prepared with the sugars, showed a lower mortality and greater resistance to subsequent injections with the live organisms than when vaccines prepared with physiologic solution of sodium chloride were used. About 500 persons immunized with Bacterium typhosum vaccine, prepared as described, showed less local and general reactions and as good an antibody response as an equal number treated with a regular formaldehydized vaccine.

DAVIDSOHN, Chicago [ARCH. PATH.]

TWO KINDS OF PRECIPITINS IN DIPHTHERIA IMMUNE SERUM. E. HOEN and L. TSCHERTKOW, Ztschr. f. Immunitätsforsch. u. exper. Therap. **70**:325, 1931.

The presence of two separate perciptins (the antibacterial and the antitoxic) is confirmed with the ring precipitation method of the authors. The bacterial precipitins were of a considerably lower titer and independent of the antitoxic qualities, which were parallel to the titer of the antitoxic precipitins. The two could be separated from each other by absorption, without influencing the titer of the antitoxin. Mixing of unheated immune serum with another heated for fifteen minutes at 65 C. removes its precipitating ability, as was shown by Schmidt and Scholtz, but with the author's method the antitoxic precipitins could be demonstrated.

DAVIDSOHN, Chicago [ARCH. PATH.]

ABSENCE OF RASH IN SCARLET FEVER IN THE AREA OF A POSITIVE DICK TEST; LIKEWISE AFTER INOCULATION WITH SCARLET FEVER ANATOXIN. A. STROE and D. GLASBERG, Ztschr. f. Kinderh. **51**:132 (May) 1931.

Four children acquired scarlet fever from four to ten days after they had shown a very positive Dick test. The sites of the reaction were free from rash, remained pale during the course of the eruption and could not be distinguished from the rest of the skin after the rash faded. A mother who had intended to nurse her child in the hospital, but because of a positive Dick test was advised to go home, returned ten days later with prodromal symptoms of scarlet fever. A second Dick test was positive and the area of reaction merged into the rash, but the site of the first test remained pale and then disappeared with the rash. The same observations held true for two children after inoculation with Dick anatoxin. It is uncertain whether specific or nonspecific factors were the cause.

EMERSON, Boston.

A STUDY OF THE CONTEMPORARY EPIDEMIC OF DIPHTHERIA AND THE CAUSES OF ITS SEVERITY: I. CLINICAL AND THERAPEUTIC STUDY. JAROSLAV PROCHAZKA, Časop. lék. česk. **68**:651 (May 3) 1929.

Both the morbidity and mortality of diphtheria made an unusual upward swerve in 1926 and 1927, with a maximum mortality of 14 per cent in 1927. The epidemic of 1926 to 1928, with its fulminating and gangrenous infections, has been the most severe in the memory of the older physicians. The etiology was not mixed infection, because the progress was identical in both the pure and the mixed cases. There was no difference in the action of the various brands of antitoxin used. Endemic malignant cases were not dependent on poor hygienic surroundings. Some of the patients, perhaps, were given antitoxin late because of obscure prodromal symptoms. A review of contemporary literature reveals a similar severity of diphtheria in other countries.

STULIK, Chicago.

THE CONTEMPORARY DIPHTHERIA EPIDEMIC AND THE CAUSES OF ITS SEVERITY: CAUSES OF DEATH. STANISLAV MENTL, Časop. lék. česk. **68**:690 (May 10) 1929.

Seventy per cent of the deaths from diphtheria occurred within seven days, with the prevalence in the 3 to 7 year group. One of these patients died of heart block, while most of those dying in the third to ninth week died of myocarditis. Practically all the children had an unusually rapid pulse rate, ranging close to 200, arrhythmia, extrasystoles, a low tension pulse, no gross cardiac dilatation and distant heart tones. Progressive laryngeal croup and bronchopneumonia were rare. Pathologic examination in the acute cases revealed normal conditions macroscopically, dilatation of the right side of the heart and contraction of the left, with no myocardial changes except in patients in whom death was delayed. The rapid elaboration and circulation of toxin in this disease produces a toxemia of all the

tissues, including the circulatory apparatus, and because of this rapid toxemia gross changes are not detected in the individual organs. Three contemporary explanations cited are: (1) myocarditis, including fiber bundle changes, (2) extracardiac nerve changes, especially in the vagus, and (3) circulatory system or vasomotor failure or injury to the suprarenals. The oculocardiac reflex of Giroux, (eyeball pressure) showed no increase in rate in 75 per cent of the severe cases, but an increase occurred in 75 per cent of the mild cases. This possibly shows a vagus toxemia in the toxic cases.

STULIK, Chicago.

THE EPIDEMIOLOGY AND PROPHYLAXIS OF SCARLET FEVER. ALOIS GUTWIRTH, Časop. lék. česk. **68**:702 (May 10) 1929.

The author summarizes the international literature up to date, noting that pseudoreactions and combined reactions are more prevalent in children giving positive Pirquet reactions; negative Dick reactions in from 90 to 100 per cent of infants under 6 months of age, even though the mothers gave positive Dick reactions, and maximal positive Dick reactions at 2 years according to Zingher, and at from 3 to 4 years according to European observers. The diagnostic value of the Dick test is slightly below that of the Schick test. The morbidity of scarlet fever has progressively increased from 2.16 to 10.57 (per hundred thousand) while the mortality has decreased from 4.1 to 1.8 per cent in the period from 1919 to 1927. The seasonal fall increase is regarded as due to school contact, even though it includes the preschool age group. The beginning of the disease is regarded as most contagious owing to the coughing of droplets of infectious material. Convalescent serum obtained from persons who have had convalescent serum should not be used, because it often produces collapse in the recipient. Dick reports as many as 91.8 per cent negative Dick reactions after inoculation with 12,000 m. c. d. (skin test doses), and the period of negative reaction is cited as from 10 months to several years by various workers. In various series, scarlet fever was from three to ten times as infrequent after vaccination as when no vaccination was performed. A bibliography is appended.

STULIK, Chicago.

THE CONTEMPORARY DIPHTHERIA EPIDEMIC AND THE CAUSES OF ITS SEVERITY: III. BACTERIOLOGY AND TOXICOLOGY; ACTION OF SERUMS. B. FEIERABEND and O. SCHUBERT, Časop. lék. česk. **68**:743 (May 17) 1929.

The original (PW8) cultures from which the antitoxin is elaborated and seventeen strains isolated during the epidemic were tested for toxicity (the ability to form toxin) and virulence (the ability to grow in spite of living tissue reaction). The specificity of diphtheria toxin and antitoxin is upheld, and it is not necessary to use new antigens in the manufacture of antitoxin. A valuable aid in determining the virulence is the simultaneous injection of the culture and antitoxin intravenously in the rabbit and intratesticularly in the guinea-pig. The gravity of the recent epidemic was due to the unusual virulence of the organism and rapid production of toxin. The previous period of safety, regarded as the second or third day, has been found to be too late in many recent cases. Alertness in diagnosis and immediate, large doses are recommended. Universal prophylaxis should be stressed.

STULIK, Chicago.

ENCEPHALOMYELITIS POSTVACCINALIS. F. S. VAN BOUWDIJK BASTIAANSE, Nederl. tijdschr. v. geneesk. **75**:586 (Feb. 7) 1931.

In 1925 the author reported thirty-five cases of diseases of the central nervous system that had followed vaccination in Holland. He now gives a description of research on these cerebral complications. Then follows a summary of the clinical results of histopathologic examination. The author makes a comparison of this type with other nonpurulent forms of encephalomyelitis. The clinical and histo-

logic differences from all other forms of encephalitis are very great. The three hypotheses of the cause of postvaccinal encephalitis are discussed, and the hypothesis of the activation of a latent virus by the vaccination is accepted as being the most probable one. The virus itself still remains unknown. In a concluding remark the advice is given to vaccinate before the age of 1 year, when the danger of encephalitis is smallest.

VAN CREVELD, Amsterdam, Holland.

DIFFERENT VACCINES FOR ACTIVE IMMUNIZATION AGAINST DIPHTHERIA. H. ALDERSHOFF, Nederl. tijdschr. v. geneesk. **75**:974 (Feb. 28) 1931.

In this clinical lecture the author gives a survey of the different methods used to obtain active immunization against diphtheria and their advantages and disadvantages. Special attention is drawn to the local reaction after the vaccination. The author gives as his personal opinion that vaccinations in general may produce such a decrease in resistance that the latent virus present causes a disease. The frequent occurrence of postvaccinal encephalitis and of other diseases after vaccination in Holland is explained by this hypothesis. The use of anatoxin is recommended for children under the age of 5 years, as the local reactions are then small and the danger of encephalitis should also be smallest. For other children toxin-antitoxin is recommended.

VAN CREVELD, Amsterdam, Holland.

Chronic Infections

THE CALMETTE-GUÉRIN STRAIN OF THE TUBERCLE BACILLUS (B C G): I. THE EFFECT IN VITRO OF ENVIRONMENT ON THE VIRULENCE OF B C G. K. T. SASANO and E. M. MEDLAR, Am. Rev. Tuberc. **23**:215 (March) 1931.

Sasano and Medlar were able to increase the pathogenicity of B C G by culture on a suitable medium to such an extent that rabbits inoculated intravenously invariably died of acute generalized tuberculosis. Control animals inoculated with the original culture grown on bile-potato-glycerin medium showed no gross evidence of tuberculosis when killed after one year. The environment that produced this great increase in virulence was a modified Sauton medium to which was added normal unheated rabbit serum. On this medium cultures at first slowly and later more rapidly became highly virulent. The essential factors of this modified medium seemed to be a careful adjustment to a p_H of from 7.2 to 7.4 and the use of fresh unheated serum. The virulence of these cultures, once established, increased with subsequent subculturing. Inoculated rabbits all showed extensive tuberculosis, with the greatest involvement in the lungs. In animals dying in from twelve to twenty-two days, bacilli were so numerous that lesions in sections stained with carbolfuchsin showed red under the low power of the microscope. An emulsion of the spleen of a rabbit dead from such inoculation produced tuberculosis in a rabbit into which it was injected intravenously. Death from extensive generalized tuberculosis resulted in five successive generations by direct animal passage from this rabbit. Further experiments showed that the altered culture of B C G was equally pathogenic for rabbits, guinea-pigs and cattle.

The authors are of opinion that since it is possible to bring about such marked alterations of B C G in vitro, and since so little is known concerning the factors that enhance or retard the pathogenicity of the tubercle bacillus, it is essential to use the greatest caution in any application of B C G as a prophylactic vaccine. While Calmette's observations point, so far, to the innocuousness of the vaccine, one must not lose sight of the fact that all control over the tubercle bacillus and its activities is relinquished once it gains access to the tissues. These investigations tend to prove that B C G is not a virus fixé, and that its stability depends entirely on its environment.

SMITH, Ogden, Utah.

EXPERIMENTAL JOINT TUBERCULOSIS: I. AN ATTEMPT TO PRODUCE LOCALIZED LESIONS IN GUINEA-PIGS. WILLIAM J. SPRING, Am. Rev. Tuberc. **23**:333 (April) 1931.

Experimental investigations of therapeutic problems in tuberculosis have suffered from two chief difficulties. It has been impossible to keep an experimental infection localized, and the wide variations occurring in untreated controls have made conclusions of doubtful statistical validity. In an attempt to produce localized lesions, three types of human tubercle bacilli, of varying virulence, were injected, in varying measured doses, into the knee joints of guinea-pigs, previously sensitized with a tubercle bacillus of low virulence. Tuberculous lesions of the synovia, and in some cases of the bone marrow, were produced, the severity of the lesions apparently depending more on the virulence of the micro-organism than on the dose within the range examined. An organism virulent enough regularly to produce joint lesions of appreciable severity usually caused severe visceral tuberculosis. In view of the wide individual variations between animals treated alike, the lesions produced are of no use for therapeutic experiments.

SMITH, Ogden, Utah.

EXPERIMENTAL JOINT TUBERCULOSIS: II. COMPARATIVE EFFECTS OF TUBERCULOUS INFECTION IN NORMAL AND PREVIOUSLY INFECTED GUINEA-PIGS. WILLIAM J. SPRING, Am. Rev. Tuberc. **23**:346 (April) 1931.

Following a single measured dose of tubercle bacilli injected into the knee joint, tuberculous guinea-pigs showed clinically an immediate inflammatory reaction more severe and of longer duration than that occurring in normal animals. Between the eighth and twelfth day in most animals, the previously normal guinea-pigs developed a secondary joint inflammation, severe and of sudden onset. This was simultaneous with the appearance of tuberculin sensitiveness in the one group tested. The symptoms of inflammation recurred also in the previously sensitized animals but much more gradually and, on the average, later. Almost to the end of the experiment the average severity of joint involvement remained somewhat greater in the previously normal animals, though the two groups overlapped widely. Until the eighty-third day the extent to which visceral tuberculosis occurred was slightly greater in the previously normal group.

SMITH, Ogden, Utah.

VITAMINE THERAPY IN PULMONARY TUBERCULOSIS: I. THE EFFECT OF ACTIVATED ERGOSTEROL ON THE CALCIUM AND INORGANIC PHOSPHORUS IN THE BLOOD-SERUM. PAUL D. CRIMM, Am. Rev. Tuberc. **23**:576 (May) 1931.

In this investigation, serum calcium and serum phosphorus determinations were employed only as corroborative of the clinical response and roentgen observations following the use of activated ergosterol as a therapeutic agent. These experiments indicate that activated ergosterol 250 D, in the dosage of 15 drops twice a day, increases the absorption of calcium and inorganic phosphorus in the gastro-intestinal tract. On an ordinary normal hospital diet it takes approximately thirty days for this dosage to produce a sustained response with these elements of the blood serum. The concentration of calcium and phosphorus furnishes a check on the symptoms of the patient during treatment. If small elevations are obtained between the sixtieth and ninetieth day of administration, together with loss of appetite, the symptoms should be used as a guide in discontinuing the drug for a rest period. The product, calcium $\times$ phosphorus, furnishes an accurate criterion for proving the effect of activated ergosterol on the calcium and phosphorus in the blood serum. Maintenance of a higher concentration of calcium and phosphorus in the blood serum below the point of toxicity produces no deleterious effect on the healing of either acute or chronic pulmonary tuberculosis. In the end it may prove to be far more efficacious in the acute disease than sunshine is in chronic pulmonary tuberculosis.

SMITH, Ogden, Utah.

TUBERCULOSIS IN ADOLESCENTS: A STUDY OF ONE THOUSAND SCHOOL-CHILDREN IN NEW YORK CITY MADE UNDER THE AUSPICES OF THE BELLEVUE-YORKVILLE HEALTH DEMONSTRATION IN 1930. MARGARET WITTER BARNARD, J. BURNS AMBERSON, JR., and MARION FRANKLIN-LOEW, Am. Rev. Tuberc. **23**:593 (May) 1931.

The two principal objects of this study were: the determination, first, of a method whereby cases of tuberculosis in children in a community like New York could be "screened out," and, second, of the incidence of tuberculosis in the child population, and the factors influencing its prevalence. All children were given periodic physical examinations, and histories were obtained from parents and by home visits. All were given at least one Mantoux intracutaneous tuberculin test (0.1 mg.), and three roentgenograms of the chest were made. The values of the various procedures in the "screening-out" process for this group were considered.

General Group Characteristics: In New York and other large cities there is so little group unity and tuberculous infection is so widespread that no one age, sex, racial or economic group could be separated that would include the greater proportion of infected children. General Health Conditions: By complete pediatric examinations alone it was impossible to predict in any way which children would be shown to have tuberculous infection. Weight: Comparisons of weight were of little value. Only about 12.2 per cent of those infected and 9.8 per cent of those with lesions were found among the children 10 per cent or more underweight. History of Household Contact with Tuberculosis: Careful investigations revealed only 99 children with actual or probable contact, and only 68 among 673 infected children. In a city like New York, tuberculous infection is so widespread that household contact is only one of many sources of infection to which children are exposed. Tuberculin Test: This was the most valuable diagnostic procedure. A total of 673 positive reactors were found in this group. By this measure children were easily separated into two classes, those with some infection needing further study and those who had had no infection or in whom complete healing had taken place. Roentgenography gives only limited information. It segregates those with demonstrable pulmonary or tracheobronchial lesions, but misses a large proportion of those infected. On the basis of these investigations, the suggested procedures for the study of a group should be as follows: Test the entire group with tuberculin; examine those with positive reaction roentgenographically; evaluate general health conditions by complete pediatric examinations; study all observations, general health conditions and environment to determine further care of reactors.

This study served to emphasize certain concepts regarding the pathogenesis of tuberculosis which are of primary importance. In all first infections of the human body with the tubercle bacilli, the regional lymph nodes of the part affected become diseased practically simultaneously. First infections usually occur in childhood, and the site of the resulting lesion is in probably 90 per cent or more of the cases, in the lungs and their regional (tracheobronchial) lymph nodes. Lymph node disease is therefore the chief problem in this group. The difficulties in diagnosis are revealed by the fact that of 623 adolescents known to be infected, examination failed to demonstrate the lesion in 489 instances. As to the potentialities concerning the persons in this group, no immediate answer is possible. The issue of human tuberculosis is a very relative thing in that it depends on a host of social, economic and personal factors as well as on anatomic, physiologic and immunologic ones, and accurate judgments must await methodical study of all of these features in every case.

SMITH, Ogden, Utah.

STUDIES OF PROTECTION AGAINST TUBERCULOSIS. A. S. GRIFFITH, M. Research Council, special report series, no. 152, 1931.

Using Macacus rhesus, the author found that the strain of B C G employed could produce local lesions, but the latter were always benign and did not lead

to generalization. Given by mouth, B C G can pass through the mucous membrane of the alimentary canal into the adjacent glands and also gain access to the blood stream. Vaccination by B C G, whether by feeding or by injection, has failed to give to monkeys the complete protection against tuberculosis reported by Wilbert, but in some instances may have produced a low grade relative immunity.

SANFORD, Chicago.

GENERALIZED TUBERCULOUS ADENITIS SIMULATING LYMPHOSARCOMA. C. DAVID MEADOWCROFT, Proc. Roy. Soc. Med. **24**:851 (May) 1931.

A girl of 8 years was said to have had an attack of mumps two years before examination. Six months later the cervical glands were noticed to be swollen. These glands gradually increased in size. At that time she was taken to the hospital where a biopsy was made and the gland was reported to be tuberculous. At the time the report was made (eighteen months later), the cervical, supraclavicular, axillary, external iliac, mesenteric and popliteal glands were all enlarged. The tonsils were still present. The spleen was not palpable. A roentgenogram showed the peribronchial and cervical glands partially calcified. Microscopic examination of the excised gland showed that it was caseous in the center with numerous giant cell systems, typically tuberculous. With Ziehl-Neelsen staining a few tubercle bacilli were found. The Mantoux test gave a marked positive reaction in twenty-four hours.

WILLIAMSON, New Orleans.

UNUSUAL CASE OF CONGENITAL SYPHILIS. H. THURSFIELD, Proc. Roy. Soc. Med. **24**:858 (May) 1931.

There were no miscarriages in the family. There were three other healthy children in the family older than the patient, who was 9 years of age. On admission to the hospital the left eye showed an opacity over the lower half of the cornea with some residual vessels suggestive of interstitial keratitis. The pharynx was covered with mucopus. The chest showed impaired resonance over the right upper lobe. The parieto-thoracic glands were enlarged on both sides. The right wrist was fixed with chronic synovitis. The left wrist was stiff. There was slight clubbing of the fingers. Roentgenograms showed rarefaction of the bones of the wrist with no erosion of articular surfaces and much fibrosis at the base and hilus of the right lung. The Wassermann reaction of the blood was strongly positive. The Mantoux test was negative.

WILLIAMSON, New Orleans.

DOES B C G REGAIN ITS VIRULENCE? CALMETTE, Bull. Acad. de méd., Paris **105**:138 (Feb. 3) 1931.

In 1928 the international conference of the League of Nations stated that B C G is harmless. This was indicated by the 320,000 vaccinated children in France and the 1,000,000 vaccinated children in the world. Even when one injects about 100 mg. of B C G into young calves nothing develops but a mild polyadenitis lasting for about three weeks. If one isolates B C G bacilli from the body of the animal one year later no increase in virulence can be demonstrated. The immunity lasts for a certain period only; after a time, revaccination is needed. Some of the French cows received a total of twelve billion germs through regular revaccinations in the course of six years. No harm was observed. At autopsy 300 children given B C G who died of different diseases in different countries showed no progressive tuberculosis that could be attributed to B C G. Zeyland in Poland performed autopsy on 56 children given B C G. The organs of 15 of them were cultured, but the isolated B C G bacilli, although they had been in the human body for six months, did not show any increase in virulence.

Some children were vaccinated by mistake with the huge dose of 30 mg. of B C G subcutaneously. No harm was observed except the local cold abscess.

Chaussinard gave 2 mg. of B C G intraperitoneally to a hydrocephalic child. In fifteen days the tuberculin test became positive. In four months the child died. Autopsy failed to reveal any signs of tuberculosis. Guinea-pig inoculations were negative.

Petroff and Watson used from 20 to 100 mg. of B C G in their experiments on animals, and reported progressive tuberculosis in from 1 to 2 per cent of the cases. No other authors described similar results. Watson and Petroff probably used already infected animals for their experiments. Petroff claimed that he was able to dissociate the B C G into virulent S and avirulent R colonies by using a special culture medium. The proportion of S : R is 1 : 50,000. Many people tried to repeat his experiments in their own laboratories, but none of them succeeded. The Robert Koch Institute in Berlin received an original S culture from Petroff himself. The investigation showed that it was not B C G but human tubercle bacilli, which means that Petroff dealt with contaminated B C G culture.

Deyer, of Oxford, stated that B C G vaccinated animals infected by a certain streptococcus showed reinoculable tuberculous lesions. He could not repeat this experiment with another B C G strain. De Saenz studied the influence of Preisz-Nocard bacilli on B C G. Under this influence the B C G rather lost its virulence than increased it. Calmette was unable to repeat Medlar's experiment which consisted of the increasing of the virulence of the B C G by the addition of unheated rabbit serum to the Sauton medium. Calmette did not succeed in increasing the virulence of the B C G by Medlar's method; neither did he succeed by culturing it in the depth of veal bouillon as Deyer did.

As to whether the Lübeck fatalities could have been attributed to an increase in virulence of the original strain, using a culture medium different from what Calmette advised, Calmette states: De Saenz, Monaldi and Zeyland proved that the sulphuric acid treatment of B C G or the presence of lactic acid (according to Hohn) does not increase the virulence. Calmette quotes Bruno Lange's letter from the Robert Koch Institute in Berlin: "1. I have used egg medium since 1927 on a certain B C G strain. After 30 transfers, in 1930, I was unable to see any increase in virulence. 2. I was unable to repeat Petroff's dissociation experiments with any success. 3. Professor Ludwig Lange found that the Hohn egg method used by Deyer does not influence the virulence of B C G." In spite of these facts, Calmette does not think it impossible that the virulence of B C G can be increased by some artificial method. This might happen just as well with B C G as with the rabies virus, which can become virulent again by transfer to rabbits. Also the smallpox vaccine can be made virulent if inoculated in horses. Similar things might happen to B C G without diminishing its value as a vaccine.

Calmette would like to have the Academy of Medicine of Paris appoint a committee, not for repeating experiments, but to get information from doctors and midwives about their seven years' experience with B C G.

KERESZTURI, New York.

ONE HUNDRED AND FIFTY CASES OF TUBERCULOUS PERITONITIS WITH TREATMENT BY HELIOTHERAPY AND ALTITUDE. CAPPELLE, Rev. franç. de pédiat. **7**:174, 1931.

From observations on 150 cases of tuberculous peritonitis in adolescents, observed at the Sanatorium d'Odeillo par Font-Romeu during a period of six years, the following conclusions are drawn: 1. All cases of chronic tuberculous peritonitis benefit markedly by a high altitude and exposure to the sun's rays. The time of exposure may be gradually increased to four or five hours a day. 2. Heliotherapy should not be given during acute manifestations, such as pain, diarrhea or a temperature above 38.5 C. (101.3 F.). 3. A laparotomy is desirable only when an acute surgical condition arises, such as appendicitis or intestinal obstruction. 4. Pleuroperitonitis is the most frequent manifestation of the onset of tuberculous peritonitis. 5. The prognosis may be judged from fluid output and intake. Eighty-two per cent of the cases were considered cured.

LESLIE, Evanston, Ill.

THE DOSAGE OF ACETARSONE. M. OPPENHEIM, Wien. klin. Wchnschr. **44**:224 (Feb. 13) 1931.

Oppenheim writes that frequent mistakes are still made in respect to the dosage of acetarsone. In recent times several injuries due to acetarsone (exanthems, vomiting, convulsions, somnolence) and even deaths after its administration have been reported which could have been avoided by correct dosage and application of the medicament. The author has never observed any injury during the seven years in which he has largely prescribed the preparation. The most important rule is to observe free intervals between the separate turns of medication, in general always a three days' pause after three days of application of the drug. The suitable dosage for the prophylaxis and therapy of syphilis is altogether as many tablets as the patient's weight in kilograms. An adult person should, for instance, be given on the first day two tablets of 0.25 Gm. each, on the second day three tablets, on the third day again three tablets followed by a three days' interval, and then once more eight tablets in the course of three days and a three days' pause until he has taken from sixty to seventy tablets according to his weight. A child suffering from congenital syphilis who weighs 3 Kg. should have three times 0.25 Gm. altogether, in small doses: on the first day about from 0.01 to 0.02 Gm., on both the second and third days 0.3 Gm., then a pause of three days, etc. In the measure as the infant puts on weight during the treatment the doses may gradually be increased correspondingly. With the exception of diarrhea (with the occurrence of which acetarsone must be discontinued) the author has never experienced disturbances.

Furthermore the method of taking the drug should be strictly observed; the whole daily dose must be taken in the morning on an empty stomach in half a glass of water; afterward the patient must not eat or drink anything for half an hour; acid foods should be avoided. Only in this way can one be sure that acetarsone is not changed too soon in the stomach. It should further be remembered that this drug has a highly toxic effect when absorbed parenterally; it was this property which prevented Ehrlich, who was the first to study the preparation, from introducing it into therapy. When erosions of the oral mucous membrane exist or when there is the possibility of a gastric ulcer being present, acetarsone should therefore be avoided. With pemphigus of the oral mucous membrane in which the drug is said to be very beneficial, the preparation should at least be swallowed quickly and large quantities of water drunk afterward so as to prevent any direct absorption in the mouth.

Every person treated with acetarsone should be kept under permanent supervision; as soon as the organism shows any warning symptom, such as irritation of the skin, rises of temperature, vomiting, lassitude or an exanthem, the administration must, of course, be discontinued immediately. There has been much neglect of these precautions also in the reported cases of injury due to acetarsone. The preparation is contraindicated (just as is arsphenamine) in cachexia, injury of the liver, idiosyncrasy to arsenic, acute and feverish infections, etc. Provided that these regulations are followed, acetarsone is valuable in the therapy and prophylaxis of syphilis and in the treatment for pemphigus. ABT, Chicago.

THE CAUSES OF THE ILLNESS IN INFANTS FOLLOWING VACCINATION WITH CALMETTE-GUÉRIN BACILLI IN LÜBECK. B. LANGE, Ztschr. f. Tuberk. **59**:1, 1930.

This is the final report from the Robert Koch Institute on the work that was done to decide what caused the death of numerous infants in Lübeck following vaccination with B C G. The conclusions are as follows: The fatalities were caused directly by the oral administration of the vaccine prepared in Deycke's laboratory. The bacilli isolated from three infants dead of tuberculosis were pathogenic and caused progressive tuberculosis in guinea-pigs. Bacilli isolated from another infant who had died of intercurrent disease were not pathogenic for

guinea-pigs. It is more than likely that the vaccines used consisted of a mixture of true B C G bacilli and a fully pathogenic strain of human bacilli. It must be assumed that the mixture was different at various times during the period of administration. There is not the slightest evidence that the B C G had increased in virulence.

PINNER, Tucson, Ariz.

BERNACKI'S REACTION IN SURGICAL TUBERCULOSIS (JOINTS AND BONES) IN CHILDREN. T. WOJCIECHOWSKI, Pedjat. Polska **10**:20 (Jan.-Feb.) 1930.

Bernacki's reaction (or the sedimentation reaction) was used on 200 tuberculous children with very accurate results as to prognosis. Bernacki's reaction can be used with as much accuracy as the Wassermann reaction in syphilis.

KRUPINSKI, Chicago.

Internal Diseases

CONGENITAL RHABDOMYOMA OF THE HEART. SIDNEY FARBER, Am. J. Path. **7**:105 (March) 1931.

A case in a 6 months old girl is reported with the following anatomic diagnosis: congenital rhabdomyoma of the heart, cerebral tuberous sclerosis, congenital polycystic kidneys, meningitis, bronchopneumonia, abscess of the lung and empyema due to Streptococcus haemolyticus. Forty-one cases in the literature are reviewed in tabular form, followed by a discussion of controversial questions. The condition is frequently associated with cerebral tuberous sclerosis and may be found in adults. The cells of the tumor are true striated cardiac muscle, but it is doubtful that the lesion is a true neoplasm. It is improbable that it arises from Purkinje fibers.

MOORE, Cleveland.

BRONCHIECTASIS. WHAT THE USE OF IODIZED OIL HAS DEMONSTRATED RELATIVE TO DIAGNOSIS BY ORDINARY ROENTGEN EXAMINATION. ADOLPH HARTUNG, Am. J. Roentgenol. **22**:120 (Aug.) 1929.

The author reports a series of ninety-two cases which were studied roentgenologically. The observations on the plain films were: (1) increased linear markings, (2) irregular densities obscuring the outline of the heart or the dome of the diaphragm, (3) irregular densities in the lower lobes, (4) a displacement of the heart shadow without demonstrable cause, (5) localized densities suggestive of atelectasis, (6) generalized densities with irregular radiolucent areas and (7) a honeycomb appearance. In about 60 per cent of the cases a diagnosis of bronchiectasis can be made from a study of the plain film. In the majority of the remaining cases, such an examination will reveal changes of a nature to indicate the probable presence of bronchiectasis, or the desirability of further investigation by bronchography. Diagnostic bronchography with iodized oil is absolutely essential for accurate information relative to the nature, location and extent of bronchiectatic dilatations.

STULIK, Chicago.

CASE OF PURPURA HAEMORRHAGICA FULMINANS. EDWARD L. BENJAMIN, Arch. Pediat. **48**:276 (April) 1931.

Nothing new is presented.

WADDELL, University, Va.

CONGENITAL ENLARGEMENT OF THE THYMUS GLAND. HENRY E. STAFFORD, Arch. Pediat. **48**:386 (June) 1931.

This is the report of a case which adds nothing to the knowledge of this subject.

WADDELL, University, Va.

THE PATHOGENESIS OF THE FORMS OF JAUNDICE. ARNOLD RICE RICH, Bull. Johns Hopkins Hosp. **47**:338 (Dec.) 1930.

This is a compact review of the physiologic pathology of jaundice which, because of its succinctness, does not lend itself well to further condensation.

Jaundice is the clinical expression of excessive retention of bilirubin within the body. Bilirubin is formed diffusely throughout the body, presumably by the reticulo-endothelial cells of the spleen, liver and bone marrow. The only known source of bile pigment is the hemoglobin of destroyed erythrocytes. This is split into bilirubin and a colorless, iron-containing fraction of whose fate little is known. Bilirubin is excreted as a threshold substance by the parenchymal cells of the liver. Once within the intestinal tract a part may be resorbed into the blood stream, but most of it is broken down by bacterial action and converted into urobilin. Of this substance the largest part is excreted into the feces. Some is absorbed into the blood stream to be reexcreted, for the most part, through the liver. Some may be retained for unknown reasons. Under pathologic conditions a considerable fraction may be excreted in the urine.

Bearing in mind this mechanism, there are four possible causes of jaundice in the absence of organic obstruction: (1) an increase in the liver threshold for bilirubin; this is entirely hypothetic; (2) an increase in the production of bilirubin beyond the power of the normal liver cells to excrete; this is rare because of the enormous reserve of the intact liver; (3) damage to the excretory integrity of the liver cells, either through functional or anatomic impairment; with certain qualifications, this is a common cause; (4) any combination of the foregoing causes; this is the common mechanism. Nearly all the factors which increase bilirubin production are accompanied by injury to the function of the liver cells.

The van den Bergh reaction enables one to measure quantitatively the concentration of bilirubin in the plasma and to determine its type, i. e., whether it is simply bilirubin which has been retained within the blood stream or whether it is bilirubin which has been excreted through the liver and then poured back into the circulation. The first is termed "indirect" bilirubin; the latter, "direct" bilirubin. According to most recent views, this difference lies not in the substance itself but in the state in which the substance exists in the blood stream, i. e., its physical state. Indirect bilirubin is said to exist in protein combination; direct bilirubin exists free. Substances that lower surface tension are capable of breaking up the protein adsorption. Certain constituents of whole bile, such as bile acids and cholesterol, have this surface tension-lowering property. Hence, the direct reaction indicates the presence in the blood stream of all the constituents of bile, whereas the indirect reaction points to an increased concentration of bilirubin alone. The third type of van den Bergh reaction, the "diphasic," is less simple of interpretation and requires for its evaluation the painstaking determination of the bilirubin, urobilin and bile acid content of the urine and the urobilin and bilirubin content of the stools.

The present classifications of jaundice, "obstructive and nonobstructive," "mechanical and dynamic" (van den Bergh), "obstructive, toxic, infectious and haemolytic" (McNee), are not satisfactory when viewed with reference to the considerations stated. When examined carefully, in spite of differences in etiology and pathogenesis, all cases fall into one of two classes: (1) those in which there is simple retention of bilirubin in the blood stream; (2) those in which bilirubin, already excreted, is regurgitated back into the blood stream together with the other constituents of whole bile. It is hereby proposed to designate the first type as "retention" jaundice and the second type as "regurgitation" jaundice. The characteristics of retention jaundice are: an indirect van den Bergh reaction; increased fecal urobilin, and an increased urobilin content of the urine, without bile salts or bilirubin. Pathologically the liver may show cloudy swelling or atrophy, but no widespread necrosis, and the bile ducts are patent. The characteristics of regurgitation jaundice are: a direct van den Bergh reaction; a decrease in fecal urobilin, and the presence of bilirubin, bile salts and occasionally uro-

bilin in the urine; pathologically there is either obstruction of the bile ducts or necrosis of the liver cells. The author then discusses the subdivisions of the various forms of jaundice.

GIARDIASIS IN CHILDREN. S. J. MCCLENDON, California & West. Med. **34**:266 (April) 1931.

Twenty-two cases of giardiasis in children are reported, five of them in detail. Common symptoms noted were: abdominal tenderness, pain, nausea and constipation, and the less definite symptoms of nervousness, irritability and easy fatigue. Diarrhea was encountered in but one case. In four patients there was an associated enuresis, which was relieved in every case when the giardiasis cleared up. All of the twenty-two patients were cured of their infection with bismuth salicylate and a product similar to acetarsone, combined with a nonirritating, low residue diet.

DICKEY, San Francisco.

THE CLINICAL ASPECTS OF DISTURBANCES OF THE PARATHYROID GLAND. J. C. MEAKINS, Canad. M. A. J. **24**:654 (May) 1931.

Clinically, two conditions are identifiable with disturbed parathyroid function: (1) a parathyroid tetany due to hypoparathyroidism characterized by a low serum calcium, a positive calcium balance and a great hypertonicity and excitability of the neuromuscular system; (2) a generalized osteitis fibrosa, a condition of hyperparathyroidism in which there are a high serum calcium, a negative calcium balance, a tendency to hypotonicity and hypo-excitability of the neuromuscular system, a pronounced rarefaction of the bones and a resorption of the corticalis and original spongiosa. A third condition, nephrosis, is mentioned. While the author believes that there is no concrete evidence that the disease is primarily due to disturbance in parathyroid function, there are two interesting disturbances in metabolism in this disease, namely, a decreased basal oxygen consumption and a lowered blood calcium. Some of these cases respond favorably to the use of parathyroid extract.

MOORE, Omaha.

THE TREATMENT OF ENURESIS IN HOSPITAL PRACTICE. S. J. USHER, Canad. M. A. J. **24**:665 (May) 1931.

A study was made of the results of treatment for enuresis in forty-eight children in the dispensary of the Children's Memorial Hospital and the pediatric outpatient department of the Montreal General Hospital. The following table shows the method of treatment and results.

Form of Treatment	No. Cases	Cure	Improved	Not Improved
Sterile water (injected)	45	24	10	11
Phenobarbital	5	..	3	2
Atropine	11	5	5	1

In addition to the aforementioned methods of treatment the mother was given specific written directions as to the method of handling the child. Stress is laid particularly on methods designed to secure active cooperation of the child. Punishing, shaming, oversolicitude, babying and similar methods are tabooed.

The authors believe from their study that psychic treatment in the form of a hypodermic injection of sterile water is a safe and valuable addition to other measures in enuresis; further, that the patients not improved by this means can in great part be relieved or cured by the administration of atropine and phenobarbital, alone or together.

MOORE, Omaha.

PURPURAS IN CHILDREN. JULIUS H. HESS, M. Clin. North America **14**:1073 (March) 1931.

In a consideration of the purpuras from the standpoint of diagnosis, prognosis and treatment, differentiation of the thrombopenic from the nonthrombopenic

types is of primary importance. In the former, the thrombopenia is the cause of the purpura; in the latter, alteration of capillary permeability is the factor. Either type may occur as the result of the action of chemical poisons (such as arsphenamine) or of infectious agents, depending on whether the injury is to the capillary wall or to the bone marrow, resulting in depression of its activity. Depression of the activity of the bone marrow as a result of infection is usually temporary. An exception is the condition termed agranulocytosis, in which the infection is usually severe and the prognosis poor.

The greatest diagnostic difficulty met with in the thrombopenic group is in differentiating purpura haemorrhagica from aplastic anemia. In the former, hemorrhage precedes the anemia, while in the latter the reverse is true. The diagnosis hinges, however, on the presence or absence of activity of the bone marrow. Examination of the blood in aplastic anemia reveals a leukopenia and a relative lymphocytosis, without signs of regeneration of the blood. In purpura haemorrhagica there is usually a polymorphonuclear leukocytosis as a response to hemorrhage, with other evidences of regeneration. However, when the bone marrow has been exhausted from repeated hemorrhages, signs of regeneration may be lacking, and in such cases, differentiation may be impossible. In both conditions the bleeding time is prolonged, and thrombopenia and deficient clot retraction are present. The pathology in aplastic anemia results from an intramedullary depression affecting the megakaryocyte, as well as erythroblastic and myeloblastic tissue, with consequent deficient formation of platelets, red cells and mature polymorphonuclear leukocytes. In purpura haemorrhagica, the thrombopenia probably results either from depression of the megakaryocytic center only or from a thrombocytolytic action of the spleen. There is no general depression of bone marrow activity.

In the nonthrombopenic group (purpura rheumatica, purpura abdominalis, scurvy, etc.) the platelets are not reduced, bleeding time is normal and the clot retracts. This is also true of hemophilia, in which, however, clot retraction may be delayed beyond the normal time.

In deciding the question of operability in purpura haemorrhagica, the following points should be carefully considered: There should be reliable evidence of activity of the bone marrow, as evidenced by (1) a polymorphonuclear leukocytosis following hemorrhage or transfusion, and (2) signs of regeneration; if anemia is present, reticulocytes must be present or increased, and nucleated erythrocytes must be present if the anemia is severe. The platelets that are present should be qualitatively efficient as determined by Howell's platelet lysis test or Birch's modification. Operation should be avoided during acute phases of the disease if possible, and the patient prepared by preliminary transfusions.

SMITH, Ogden, Utah.

RHEUMATIC FEVER, SUBACUTE BACTERIAL ENDOCARDITIS AND FOCAL INFECTION. JESSE F. GERSTLEY, M. Clin. North America **14**:1221 (March) 1931.

A boy of 13 years had a subacute bacterial endocarditis developing on a chronic one, probably of rheumatic origin. The tonsils had been removed many years before admission. Extraction of one badly diseased tooth was not followed by any noticeable reaction. Cerebral embolism and death occurred directly after extraction of the second tooth a few months later.

The cardiac changes found at autopsy were: acute vegetative and ulcerative endocarditis of the mitral valve, superimposed on a chronic endocarditis; acute parietal endocarditis of the left auricle and acute myocarditis. No Aschoff bodies were found. Clinically, however, the earlier cardiac changes were unquestionably rheumatic.

The advisability of operative intervention for the removal of foci of infection in acute conditions is questioned. In this case a cerebral embolism occurred the day following the extraction of the second tooth. The patient had suffered from emboli and infarcts, however, previous to this time. Nevertheless in view of the

almost certainly fatal course of his disease, it was felt that the risk was justified. In this case the teeth, suspected of harboring the infection, could not positively be implicated. Cultures from the root of the second tooth revealed a streptococcus, but it was not identical with the one found in the blood and on the heart valves.

SMITH, Ogden, Utah.

VASCULAR AND CEREBRAL COMPLICATIONS OF NEPHRITIS IN CHILDREN. HUGH L. DWYER, South. M. J. **24**:534 (June) 1931.

The author recommends frequent blood pressure examinations of all children with acute hemorrhagic nephritis. A rising blood pressure in the presence of headaches, vomiting or visual disturbance is a warning of cerebral involvement. Cerebral complications in nephritis characterized by convulsions without an accumulation of nitrogenous products in the tissues, so-called convulsive uremia, are due to edema of the brain. Magnesium sulphate solution by mouth and by vein decreases the cerebral edema, resulting in a disappearance of the symptoms of increased intracranial tension and a drop in blood pressure. In nephritis of long duration a persistent elevation of blood pressure denotes serious disease of the kidney.

Extreme degrees of hypertension with arteriosclerosis in children may be of two kinds: (1) those secondary to disease of the kidney, and (2) those in which the renal disease appears to be secondary to a generalized vascular sclerosis.

SCHLUTZ, Chicago.

CAPUT OBSTIPUM CONGENITUM. LUTHER W. HOLLOWAY, South. M. J. **24**:597 (July) 1931.

The author is of the opinion that caput obstipum of the sternocleidomastoid muscle is a clinical entity and is not a hematoma. Caput obstipum is usually followed by wryneck. The condition should be treated actively and not expectantly. The injection of a 1 per cent solution of pepsin in Pregl's iodine solution, according to the formula of Payr, has been recommended.

SCHLUTZ, Chicago.

FRAGILITAS OSSIUM IN TWINS: CASE REPORT. J. NEWTON SISK, Wisconsin M. J. **30**:272 (April) 1931.

Fragilitas ossium, a hereditary disease, without a break in antecedent continuity and transmitted by either parent, occurred in twin girls. Roentgenograms and photographs of them at the age of 4 years are shown. Both had fractures of the femur and of the lower ribs. Some of these were united and some not united. They had blue sclerae and arcus senilis. In addition to these symptoms, their father also had otosclerosis.

JANNEY, Milwaukee.

A CASE OF CALCINOSIS UNIVERSALIS AND A SUGGESTED METHOD OF TREATMENT. JOHN CRAIG and ALEXANDER LYALL, Brit. J. Child. Dis. **28**:29 (Jan.-March) 1931.

The history is that of a girl aged 5 years and 3 months in whom, a year previously, swelling of the legs developed from below the ankles to above the knees which subsided in the course of three months. On admission to the hospital "hard lumps could be felt under the skin all over both legs, and small scattered lumps in the thighs, arms and in the left malar region." The masses gave shadows on roentgen examination. Except for enlarged and unhealthy tonsils the physical examination gave negative results. The blood calcium was 10.2 mg. per hundred cubic centimeters, and the blood phosphates 3.92 mg.

After failure of treatment with iodides and massage, disodium phosphate was given by mouth with decided beneficial effect. Unfortunately no further blood

calcium or phosphate determinations were done, but the authors quote the observations of other investigators to the effect that a fall in serum calcium follows the exhibition of phosphate either intravenously or by mouth.

LANGMANN, New York.

BACTERIAL OR INFECTIVE ENDOCARDITIS. GIBSON LECTURES FOR 1930. WILLIAM S. THAYER, Edinburgh M. J. **38**:237 (April) 1931; 307 (May) 1931.

Thayer, of Baltimore, in his first Gibson lecture at the University of Edinburgh, has drawn on the statistics of forty years at the Johns Hopkins Hospital, as well as his considerable outside experience. Fatal acute rheumatic endocarditis is, above all, an acute, rapidly fatal disease of early youth; 72.3 per cent of sixty-five autopsies were on patients in the first and second decades of life. Antecedent rheumatism or chorea had occurred in 77.4 per cent, while evidence of chronic heart disease was found in 83 per cent at autopsy. Fourteen patients gave a history of no rheumatism or chorea, but chronic rheumatic changes were present at autopsy. This acute rheumatic cardiac disease, therefore, produced such mild manifestations in these young patients as to be unrecognized during life. Thayer's experience points to the important rôle of persistent or unexplainable fever in chorea as indicating cardiac disease. Foci of streptococcal infection were present as the rule. Forty-eight of fifty cases showed tonsillar, adenoid or peridental infection. Pericardial disease was recorded in 84.6 per cent of the cases. The old French term "endopéricardite" is justified in the adherent type of serofibrinous pericarditis resulting in synechiae, a striking feature of rheumatic heart disease. Also Aschoff bodies (the acute perivascular nodules) were present in the heart muscle in nearly all cases. Among other changes is the interesting acute rheumatic lesion in the endocardium of the left auricle near the mitral valve, noted as a scar by Lépine in 1869, and as of a rheumatic nature by MacCallum in 1924.

Congenital malformation of the aortic valves (showing bicuspid aortic cusps) has been reported as complicated by bacterial endocarditis in a considerable percentage of cases by other observers. Thayer reports in his ninety-nine instances of acute and subacute endocarditis examined after death that 7 per cent showed evidence of congenital defects at the location of the diseased condition.

In his second Gibson lecture, Thayer relates his experience with endocarditis due to other of the commoner organisms. Subacute vegetative endocarditis may be due also to the gonococcus, Staphylococcus albus, rarely Staphylococcus aureus and the pneumococcus. The bacillus of Pfeiffer caused an endocarditis in nine instances (seven proved at autopsy), which is entirely similar to subacute streptococcal endocarditis, in that there were exuberant granulations and the lesions showed the same distribution. These granulations were filled with characteristic small gram-negative bacilli. The lesions in one instance were found on an area of congenital pulmonary stenosis. In the series there were no children in the first decade of life and but one in the second.

Pneumococcal endocarditis occurred twice during the first decade, in the total of forty-two cases, so that it is a process occurring as a rule much later in life than does streptococcal heart disease. In two instances congenital malformation of a bicuspid aortic orifice had pneumococcal endocarditis engrafted on it. Previous rheumatism or chorea is found in the history much less frequently than in the streptococcal series.

One of the thirty-two cases of gonococcal endocarditis was in a child. Gonococcal infection of the heart involves the right side more frequently than does streptococcal infection. In infection by the gonococcus, as in that by the pneumococcus, the aortic valve and next the mitral valve are the ones generally attacked.

In the series of thirty-two cases due to Staphylococcus aureus, four were in the first decade and seven in the second, making about one third of the total number. The disease is in an accompaniment of general sepsis and always fatal. Preexisting rheumatism or syphilis is not proved to play any rôle in predisposing to this type of endocarditis.

In the treatment for infective endocarditis, one can say at present that scrupulous general care produces the best results, following the principle of nil nocere.

NEFF, Kansas City, Mo.

PUNCTATE BASOPHILIA: A METHOD FOR EASY DEMONSTRATION BY DARK GROUND ILLUMINATION. W. T. NELSON, M. J. Australia **1**:310 (March 14) 1931.

The use of dark-field illumination in the microscopic examination of blood films for evidence of punctate basophilia was investigated by the author and found to be an accurate method, having the advantage of being far less fatiguing and time-consuming than bright-field methods in counting stippled cells in blood films. However, in comparing the two methods, many more stippled cells were found by the dark-field than by the ordinary method. Counts running up as high as several thousand stippled cells per million red cells were found in apparently normal persons and in persons with various diseased conditions as well as in trinitrotoluene workers. Because of the unexpectedly high percentage of persons in whose blood evidence of stippling may be found by the dark-field method the author believes that in any individual case the significance of this change as evidence of trinitrotoluene or lead absorption is questionable.

GONCE, Madison, Wis.

PERSISTENT PYREXIA: (?) STILL'S DISEASE. H. J. STARLING, Proc. Roy. Soc. Med. **23**:1577 (Sept.) 1930.

A girl aged 15 years was admitted to the hospital in April, 1928. On admission she looked pale and ill, and her head was bent forward owing to fixation of the cervical vertebrae. The mouth could be opened only three fourths of an inch, and the left wrist was completely ankylosed. All the joints showed limitation in movement. For the last two years she had suffered from persistent pyrexia. She remained in the hospital for seven months, during which time the tonsils were removed and she was treated with polylavent antirheumatic vaccine and intramuscular injections of peptone. On discharge she was immensely improved. She was readmitted in September, 1929, suffering from a relapse.

WILLIAMSON. New Orleans.

COELIAC DISEASE. H. J. STARLING, Proc. Roy. Soc. Med. **23**:1580 (Sept.) 1930.

A case of celiac disease was reported in a boy aged 11½ years.

WILLIAMSON, New Orleans.

CONGENITAL HEART DISEASE. H. J. STARLING, Proc. Roy. Soc. Med. **23**:1582 (Sept.) 1930.

A case of congenital heart disease was reported in a boy aged 8. He had suffered from severe epistaxis since he was 6 weeks of age, which would necessitate complete rest in bed for three or four days. In the intervals he would play games at school, but suffered from shortness of breath. On examination the heart was enlarged and there was a loud systolic blow transmitted to the right of the lower sternum. At the third left interspace there was a harsh systolic rumble, then a second heart sound followed by a diastolic blow. These sounds were transmitted chiefly upward and to the left. The face was flushed and the eyes were prominent. It was suggested that pulmonary stenosis and regurgitation were present.

WILLIAMSON, New Orleans.

HYPERTHYROIDISM. DONALD PATERSON, Proc. Roy. Soc. Med. **24**:569 (March) 1931.

A case of hyperthyroidism was reported in a girl aged 10 years.

WILLIAMSON, New Orleans.

THROMBOCYTOPENIC PURPURA. DONALD PATERSON, Proc. Roy. Soc. Med. **24**:571 (March) 1931.

A girl, aged 6 years, was admitted to the hospital with a history of severe attacks of epistaxis for two weeks. There were a few scattered petechiae on the back, abdomen and thighs. The spleen was not palpable. There was a basal systolic murmur. The blood count showed: red blood cells, 2,143,000; hemoglobin, 45 per cent; polymorphonuclears, 62 per cent; lymphocytes, 32 per cent, and platelets, 125,000. Splenectomy was performed two days later, transfusion being done both before and after the operation. Epistaxis recurred frequently after the operation, often necessitating transfusion. The coagulation time remained normal throughout. The bleeding time varied from seven and a half to twenty-three minutes. The author felt that the operation had not helped; in fact, he thought that it had made the child worse.

WILLIAMSON, New Orleans.

RHEUMATIC AORTIC STENOSIS. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **24**: 854 (May) 1931.

A girl aged 15 had complained of pains in the joints at the age of 10 years, and had had tonsilitis at the age of 12. The tonsils and adenoids were removed in 1928, the operation being immediately followed by scarlet fever. The patient was first seen by the author in 1928, when the heart showed diastolic and systolic murmurs at the aortic area and to the left of the sternum. A year later, an aortic thrill was felt in the aortic area and the systolic murmur became louder. Cardiac enlargement was present and was increasing. The pulse was anacrotic. The patient kept well and at work for two years. She is now suffering from fainting spells and numbness of one side of her body. The author believes that this is due to small emboli lodging in the sensory area of the brain. He also believes these cases to be rare. He saw a series of 550 cases of all types of rheumatic carditis in five years and saw aortic stenosis in only two instances.

WILLIAMSON, New Orleans.

THROMBOCYTOPENIC PURPURA. DONALD PATERSON, Proc. Roy. Soc. Med. **24**: 856 (May) 1931.

A case of thrombocytopenic purpura was reported in a child aged 7 years. The report is accompanied by repeated blood pictures, made during the child's stay in the hospital.

WILLIAMSON, New Orleans.

PHYSIOLOGIC AND PATHOLOGIC RÔLE OF THE THYMICOLYMPHATIC SYSTEM. G. MOURIQUAND AND M. BERNHEIM, Arch. de méd. d. enf. **34**:205 (April) 1931.

In an exhaustive monograph these distinguished French clinicians review this problem from every conceivable angle. Histologic, histophysiologic, biochemical, physiologic and pathologic data are assembled and surveyed carefully for evidence to support the prevailing opinion that in some obscure way the thymicolymphatic system may exert a profound influence on the vital processes.

Their conclusions are extremely frank and interesting; the authors believe that no clear case can be made for a "thymicolymphatic system," either in its embryology, its histology or its physiology. The only approach of the two structures lies in their biochemical constitution. While it would be difficult to deny thymic hypertrophy and enlargement of the lymph glands and spleen, frequently associated with spasmophilia and favorable to sudden death, the rôle of thymic hypertrophy in this syndrome is at least controversial. Assigning the cause of sudden death to the thymus is a doubtful expedient and should probably be replaced by the consideration of an obscure vital disequilibrium, or "the diathesis for sudden death" whose essential elements are still unknown. The origin of this thymicolymphatic

state will eventually be traced, the authors believe, to a congenital defect acquired in utero under the action of factors possibly infectious. In any event, the victim of the disorder is born with a special dystrophy favoring sudden death.

AMESSE, Denver.

TWO CASES OF PERNICOIUS APLASTIC ANEMIA WITH FEVER IN INFANCY. R. A. MARQUÉZY and P. FLANDRIN, Arch. de méd. d. enf. **34**:288 (May) 1931.

Pseudoleukemic anemia of von Jaksch is the common form of grave anemia in childhood; pernicious anemia of Biermer is excessively rare. In contrast, pernicious aplastic anemia, found exceptionally in adult life, is relatively more frequent in the infant.

The authors report two fatal cases of this disorder, which resisted all methods of treatment and ran a rapid course. The first observation was in a boy of 4 years, whose history showed he had always been pale. He was taken sick in July, 1930, and entered the hospital on September 17, with profound anemia and with a temperature ranging from 104 to 105 F.; there were purpuric spots and ecchymoses disseminated over the entire body, and his general aspect was one of grave intoxication. The blood picture showed 930,000 red cells, 25 per cent hemoglobin and 7,200 white cells, of which 22 per cent were large mononuclears. In spite of repeated transfusions the patient grew progressively worse and died on October 4.

The second case was that of a boy aged 14 years, admitted to the hospital in coma with subcutaneous hemorrhages and hyperpyrexia. The child was an orphan, and no family or personal history was obtainable. The course of the disease was much similar to that of the previous case, and death ensued in eleven days. Autopsy demonstrated many suffusions of blood over the abdominal and thoracic viscera, with enlargement of the liver and degeneration of the osseous marrow. In discussing the therapeutics of aplastic anemia the authors stress the utter uselessness of liver in any form, and present this fact as a means of differential diagnosis.

AMESSE, Denver.

RETICULOCYTOSIS IN THE COURSE OF HODGKIN'S DISEASE. C. M. LAUR and NOËL FIESSINGER, Compt. rend. Soc. de biol. **106**:1147 (April 24) 1931.

In line with B. Kinia of Vienna the authors found reticulocyte counts of 11.5, 7 and 6.6 per hundred red cells as compared with the normal count of from 0.3 to 1.0, in four cases of Hodgkin's disease.

WAHL, Cleveland.

RELATION OF VAGOTONIA TO HYPERTROPHY OF THE THYMUS. H. LEMAIRE, Nourrisson **19**:145 (May) 1931.

Sudden death in infants may occur either from hypertrophy of the thymus or from vagotonia. The author does not believe that there is any relation between the two conditions. Several cases are cited. The article appears posthumously.

MCCLELLAND, Cleveland.

STUDY OF THE CONSTITUTIONAL DEFICIENCY OF INFANTILE HEMATOPOIESIS. FERRUCCIO ZIBORDI, Clin. pediat. **13**:405 (May) 1931.

The author discusses the reaction of the human organism in certain infantile hematopoietic insufficiencies, including general hematopathies as well as so-called secondary anemias. Data and personal experiences are presented in an endeavor to establish the extent to which the organism influences the appearance and evolution of the pathologic variations affecting infantile hematopoiesis. He submits a "stimulation test" by which the hematologic behavior of children may be studied so as to recognize those having an insufficient hematopoietic reaction.

SIGNORELLI, New Orleans.

VACCINOTHERAPY IN INFECTIONS OF THE URINARY TRACT IN INFANCY. LUIGI AURICCHIO, Pediatria **39**:457 (May 1) 1931.

This paper represents a report of results obtained in the treatment of seventy-two patients with various infections of the urinary tract by the use of autogenous vaccines. Complete cures were obtained in sixty-nine cases; of the other three, one was complicated by the coexistence of an active tuberculous infection; one by the coexistence of syphilis and the third by the presence of a congenital malformation of the urinary tract. Various micro-organisms were represented in the series, the most frequent being Bacillus coli, Staphylococcus aureus and Staphylococcus albus, alone or in combination. Results were uniform and were checked both clinically and microscopically.

The author concludes that autovaccinotherapy is the most valuable method of treatment in all infections of the urinary tract, and he recommends its use not only in the chronic cases and in those that have failed to respond to a liberal administration of the usual antiseptics, but particularly in cases that are severe from the onset.

SIGNORELLI, New Orleans.

Nervous Diseases

THE AFFECTIVE PSYCHOSIS IN CHILDREN. J. KASANIN, Am. J. Psychiat. **10**:897 (May) 1931.

The child has no capacity for analyzing his emotions and cannot express them verbally. He merely states, if anything is wrong, that he does not feel well, and this is usually taken as a physical complaint; the true nature of the illness is not suspected. The clinical picture of a manic disorder in children consists of mild elation, overactivity, irritability and a push of speech. In the depressive stage there is withdrawal, undertalkativeness, general retardation and occasional refusal of food. This study is based on an analysis of ten cases, six boys and four girls. It represents a four year period of child admissions to the Boston Psychopathic Hospital.

Among etiologic factors, the exciting causes of the elation or depression may be very trivial. Among the contributing causes must be mentioned: physical defects and anomalies differentiating these children from their playmates (five cases), heredity (three cases) and mismanaged sex life (three cases). Defective disorders in childhood involve a serious prognosis. Recurrences of attacks are common. Although intellectual deterioration is not common, there is a certain lack of curiosity, a retardation of progress and loss of childhood spontaneity.

JAHR, Omaha.

ROENTGENOLOGIC STUDY OF THE COLON IN A CHILD WITH A SPINAL CORD LESION. HARRIET CARSWELL MCINTOSH, Am. J. Roentgenol. **32**:247 (Sept.) 1929.

The author's summary is as follows: "A case is presented, of a boy of six years, with a 3 plus Wassermann reaction and a history of poliomyelitis, having a spinal cord lesion unsatisfactorily localized, but known to include to some degree the lumbosacral segments, with involvement of both motor and sensory fasciculi within the cord. He has a gaping sphincter, with loss of sensation in the rectum and around the anus. There is some incontinence. A gastrointestinal study by the roentgen ray shows a marked colonic stasis, a barium meal requiring twelve days to reach the rectum, and longer to be completely expelled. The retardation is chiefly in the distal colon. There is no localized dilatation or atony of the large gut, no cecal stasis, and no rectal stasis (dyschesia). The tone of the entire colon is good; the haustra are normal. The fault is believed to be chiefly a sensory impairment at the anal end of the tube, resulting in a complete absence of mass movement."

STULIK, Chicago.

ON THE NATURE OF FITS. FOSTER KENNEDY, Bull. New York Acad. Med. **7**:221 (March) 1931.

Epilepsy is not a disease but the expression of an induced or an innate instability of the nervous centers due to many causes, operating probably through a common mechanism. The causes are protean, covering a wide range of conditions sometimes determinable but most frequently obscure and often fleeting. Not all convulsive seizures, regardless of epileptiform manifestations, are true epilepsies. Fits occasionally complicate renal disease and uneasy pregnancies. These convulsions yield to treatment that tends to eliminate the poisonous materials from the system. Epilepsy does not, contrary to current impressions, generally terminate in dementia.

The author presents a clear and concise discussion on the physiology of the epileptic state with logical comparisons and relationships to other mental states not so well recognized. With the cortical inhibitions impeded, the lower neuronic levels pour downward an ungoverned stream of tonic impulses representing decerebrated rigidity. The phenomena of petit mal, migraine, recurrent syncope, mental states of unreality, a sensation of mediastinal oppression with fear of impending death associated with transient seizures of cardiac gallop or pseudoangina, are analogous spectra of epilepsy. Interesting illustrations are offered in support of this statement. Vasomotor fluctuations are direct causes of the fit, regardless of apparent or obscured basic factors (cerebral trauma, toxemia or metabolic disorders).

In the treatment for epilepsy, no one program can be expected to yield favorable results in all cases. The aim should be: first, to raise the threshold of neural explosion, and second, to minimize the "detonating stimuli likely to reach it." Again, the patient should receive more attention than the "fit." Every effort should be made to help the patient with his environmental problems, interests, discipline and habits, and to aid him to live "with fair weather in his soul."

JAHR, Omaha.

THE CRIMINAL FEEBLEMINDED. F. C. RICHMOND, J. Am. Inst. Crim. Law & Criminol. **21**:537 (Feb.) 1931.

Richmond, who is director of the Wisconsin Psychiatric Field Service, states his belief that the public is either uninformed or misinformed concerning the prevalence and importance of the factor of mental deficiency as predisposing to delinquency and crime, and that only to a limited extent in New York and Massachusetts is the problem adequately dealt with by law. He asks a number of pertinent questions and draws attention to certain parallel aspects of mental disease and mental defect which provoke different reactions on the part of individuals and of organized society.

Any legal classification of the criminal feebleminded must of necessity be based on the statutes, and judicial opinions are cited with special reference to the statutes of Wisconsin. Consideration is then given to the adequacy of various psychiatric definitions and classifications of feeblemindedness and to the subject of mental testing or psychometry. The following definition is offered: "The criminal feebleminded are those persons under or within the jurisdiction of penal, reformatory or correctional agencies or institutions showing an intelligence quotient not above seventy-five, whose low mental level is due to arrested development."

The cause and incidence of feeblemindedness are discussed from the psychiatric standpoint, including new data covering examinations made in Wisconsin during the four year period from July 1, 1926 to June 30, 1930. From his data, Richmond draws the conclusion that the proportion of feebleminded among criminals and delinquents increases progressively as the age scale ascends, and that feeblemindedness is one of the outstanding factors, second only to broken homes, in the production of criminals and delinquents.

The following are selected quotations from volume 10 of "The Medical Department of the United States Army in the World War" to establish and confirm Richmond's stated belief: "Of the disciplinary cases reported by neuropsychiatrists, 42.3 per cent were mental defectives." "It was believed that no other class of men made for so much mischief in the Army as did the feebleminded." "There are sufficient grounds for excluding all mental defectives from the military forces except when the last available man power must be utilized." The question of legal responsibility of feebleminded persons for criminal acts is given extended consideration, and the present psychiatric trend in the direction of treatment and training, rather than of punishment, is stressed. Division of the criminal feebleminded is made into two classes: first, the potential delinquent, who requires protection, special training and supervision, and second, the confirmed or habitual delinquent, who requires segregation during which training, study and observation are combined with a view to returning to the community those who are selected as the most favorable risks.

Quotations from the literature are numerous and well selected; they include the modern program outlined in Davies' "Social Control of the Mentally Deficient," to which program the author adds the following: "The feebleminded inmates of penal, reformatory and correctional institutions serving sentences for felony shall prior to expiration of sentence be formally adjudged to be mentally deficient and as such committed to a proper institution. Those whose mentality is so deficient or whose delinquency is so chronic that their return to the community is contraindicated should be detained indeterminately, while those whose return to the community shall come to be considered practical would, following sterilization, be paroled indeterminately under the supervision of the law." In support of his final recommendation, Richmond states that mental deficiency, when not acquired, is transmissible from parent to child as a recessive characteristic male dominant by social selection obtained in mating.

WILLEY, Harrisburg, Pa. [ARCH. NEUROL. & PSYCHIAT.].

THE MENTAL CAUSES OF CHILD ACCIDENTS. HERBERT J. STACK, Ment. Hyg. **15**:283 (April) 1931.

The most important approach to the problem of preventing accidents among children is that of mental hygiene. The mental factors that may represent the underlying causes of accidents include worry, fear, rebelliousness, adventurousness, stupidity and fatigue. Worried children are often anxiously hurrying to get somewhere; they are apt to be less alert. Rebellious children resent safety instruction and are apt to court danger as a gesture of defiance; adventuresome boys may seek the thrill of jeopardizing their limbs in street traffic. Fatigue commonly underlies accidents, and it is a fact that most accidents to children in the streets occur in the late afternoon. Stupidity bears an uncertain relationship to the danger of suffering an injury; certainly the feebleminded child is more apt to get into trouble than the normal one, but within the limits of normal intelligence it has never been demonstrated that caution and mentality are proportional. The school, the home and the community in general must provide opportunities for real but relatively safe adventure for children and must cultivate in its future citizens a healthy and intelligent respect for danger.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.].

EXAMINATION OF THE SO-CALLED "BAD" OR "NERVOUS" CHILD. FREDERICK L. PATRY, New York State J. Med. **31**:809 (July 1) 1931.

The school physician should make a thorough study of these cases. The visiting teachers, parents, attendance officers and friends can assist in collecting the necessary facts.

AIKMAN, Rochester, N. Y.

CLINICAL VALUE OF A NEW REFLEX IN CHOREA. G. A. STEPHENS, Brit. M. J. **1**:303 (Feb. 21) 1931.

The author finds what he calls the dorsal reflex in most choreic patients. There is hypersensitiveness on both sides of the spine, usually from about the third dorsal level and extending down to the buttocks; when the skin in this region is picked or scratched there is contraction of the underlying muscles. The author does not find this reflex in patients suffering from acute rheumatism and acute carditis. He is of the opinion that chorea really represents a toxemia, primarily dependent on calcium deficiency. Physiologic changes dependent on altered calcium metabolism affect primarily the vascular system, causing a diminished supply of blood to the muscles and vital organs and thus producing the mental changes and the choreic effect on the muscles. In his opinion, chorea is a sort of Raynaud's disease or "spasm" of the arteries of the brain. Thus, in regard to the "choreic reflex," the author believes that it suggests some interference with the blood supply to the afferent parts of the nervous system, especially in the neighborhood of the midbrain, and concludes: "The fact that I have seen this dorsal reflex in a case of encephalitis tends to support my doctrine." The essential aspect of the therapy advised is the administration of calcium lactate and parathyroid extract.

FERGUSON, Niagara Falls, N. Y. [ARCH. NEUROL. & PSYCHIAT.].

CONGENITAL ANEURYSM OF THE BRAIN. HUGH REID, Brit. M. J. **1**:445 (March 14) 1931.

The clinical history and syndrome and the necropsy obervations are given in the case of a woman, aged 33, who died of a ruptured congenital aneurysm at the base of the brain. The patient had been well until a month before death, when she had had a slight attack of vomiting and had complained of vague headaches. Vague symptoms persisted. Eight days before death, she fainted twice and vomited without warning. The following week, she had a low occipital headache and pain in the back, and felt feverish. Then suddenly she collapsed and became comatose. The muscles were flaccid, and all reflexes absent. The pupils were widely dilated. She died about seven hours later in coma.

At necropsy, a small saccular aneurysm, 1 by 0.05 by 0.05 cm., was found occupying the space between the two anterior cerebrals and springing from the junction of these arteries. It had ruptured on the lower side. There was an old fibrous clot which evidently represented the remains of an older hemorrhage.

The author gives the clinical symptoms of congenital aneurysm prior to rupture and those following rupture. Before rupture, localizing symptoms may be recognized from pressure on neighboring structures, dependent on the location of the aneurysm. For example, those of the anterior half of the circle of Willis may cause irritation of the second, third, fourth, fifth or sixth nerves. One reported case showed only trigeminal neuralgia. An irregularity of the pupil on one side may be the only sign. In the posterior half of the circle of Willis, pressure on the brain stem, in addition to paralysis of the last four cranial nerves, might give rise to paraplegia, cerebellar symptoms, dysarthria, dysphagia or contralateral hemianesthesia.

After rupture, leakage of blood into the subarachnoid space at the base of the brain produces clinical signs on which a diagnosis may be made with reasonable certainty. The authors add, however, that in some cases meningitis or influenza may be closely simulated. The symptoms are dependent on the rate of the hemorrhage. Loss of consciousness passes on to deep coma with a severe hemorrhage, while with a small one, giddiness, headache and vomiting may be the only effects. Moderate pyrexia, stiffness of the neck and a positive Kernig sign may be present. In these latter cases, a differential diagnosis from meningitis is made by an examination of the cerebrospinal fluid and the suddenness of onset.

FERGUSON, Niagara Falls, N. Y. [ARCH. NEUROL. & PSYCHIAT.].

THE OCCURRENCE OF INTRANUCLEAR INCLUSIONS IN THE NERVE CELLS IN POLIOMYELITIS. E. W. HURST, J. Path. & Bact. **34**:331, 1931.

The bodies described are probably nuclear inclusions of the same order as those in herpetic encephalitis, Borna's disease, etc.; they are, however, much less numerous, smaller and more difficult to stain electively than these other inclusions. They can be distinguished from the acidophilic masses normally present by their greater sharpness of outline and their more solid appearance and by the fact that under conditions leading to their appearance the acidophilic coagulum is wanting in whole or in large part. Their paucity and the limited time during which they can be found do not favor a study of their evolution, but it seems possible that they may represent a nuclear reaction to the attack of the virus. It is known that after intracerebral inoculation the virus does not reach the cord, at least in detectable amount, until immediately before the onset of paralysis (Fairbrother and Hurst, 1930); the bodies have never been found during the incubation period. They occur always in damaged cells but, on the other hand, they have not been seen in completely necrotic cells. In the poliomyelitis of monkeys, a considerable proportion of the anterior horn cells undergo complete necrosis within a few hours of the onset and do not necessarily pass through a phase of degeneration in which the bodies are present; indeed, the latter may develop only in cells that possess rather more power of resistance to the virus and that consequently degenerate more slowly. However this may be, they have not been seen in markedly degenerate cells in the cords of rabid monkeys or in a series of other pathologic and normal tissues. Similar bodies were present in the only human case examined and as far as this limited evidence goes they appear to be characteristic of the disease.

AUTHOR'S SUMMARY.

NEW FAMILIAL MALADY CHARACTERIZED BY A CONGENITAL CATARACT AND AN ARREST OF SOMATO-NEURO-PSYCHIC DEVELOPMENT. G. MARINESCO, S. DRAGANESCO and D. VASILIU, Encéphale **26**:97 (Feb.) 1931.

Case material is presented of a new type of congenital or familial condition that has not been described in the literature. Case 1, presented in considerable detail, shows: a bodily development giving the impression of a child aged 8 or 9 years, whereas the chronological age is 18; practically no evidences of pubertal changes; a certain degree of edematous infiltration of the skin; some rachitic deformations; bilateral cataract, and a slight horizontal instability of the eyes. The patient sits on the bed, with the head inclined, a picture of stereotyped immobility; walking is difficult; motor power is decreased, and hypotonia general. Sensibility is normal. Mentally, the patient can carry out simple commands. The case may be summarized by saying that it is a retardation in somatic and neuropsychic development, accompanied by bilateral cataract, dating from the first year of life. Case 2, that of a brother, aged 17, is also presented in considerable detail. It is characterized by bilateral cataract, comparative immobility, poverty of spontaneous movement, inexpressive physiognomy and imbecility. Case 3, that of a child 8 years of age, shows the same type of arrest in somatopsychic evolution. In this case a biopsy of the right frontal lobe was performed. The architecture was normal and the layers were well developed. Chromatophil substance was diminished. Some of the cells in layer 3 were elongated, with the nucleus pushed nearer the periphery and with the dendrites unusually prominent. With Cajal stains, two kinds of cells were sharply differentiated, a clear and a dark type. The latter cells occupied almost the whole microscopic field. Microglia was without manifest alterations. With Scharlach's stains a lipoidal disintegration was demonstrated in the basal part of the dendrites. The general histopathologic picture was one of a degeneration rather than an inflammation. Case 4, that of a child aged 4, is also included. In physical appearance and development she appears half this age; she cannot stand alone.

Wassermann tests give negative results in all, but in three of the children the reaction of Prunell, which some authorities consider as specific for hereditary syphilis, is positive. Estimations of blood calcium show: in the father, 7.76 mg.; in the mother, 10.99; in case 1, 8.53; in case 2, 6.9; in two normal children in the family, 9.2 and 6.7 mg. (normal from 10.5 to 12 mg.).

The authors summarize as follows: This is a familial condition, affecting several children in a family, characterized by the appearance of cataract, a retardation in somatic development, the presence of neuropsychic disturbance, and a hypocalcemia; one must admit that this last feature is constitutional because it is present even in brothers who are apparently sound, and in one parent. There are three possibilities of interpretation: a primary endocrine disturbance with secondary cerebral manifestations, an infantile encephalopathy with consecutive endocrine modifications, or a simultaneous disturbance of the nervous system and of the glands of internal secretion. Arguments for these various points of view are presented, with citations from the literature.

ANDERSON, Los Angeles [ARCH. NEUROL. & PSYCHIAT.].

CHRONIC CHOREA AND ITS RELATION TO THE STRIATUM. L. TOKAY, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:209 (Oct.) 1930.

This paper is based on a review of the literature on chronic chorea and a clinico-anatomic study of two personal cases observed by the author.

Case 1 was that of a woman, aged 71, in whom chronic progressive generalized chorea developed at the age of 56. The chorea was associated with a progressive mental weakness, which, though definite, was not severe. In conformity with the reports in the literature, in this case the changes in the cells were also marked; they were not senile changes, but were definitely degenerative. The degeneration had progressed to destruction, which was most marked in the third layer of the cortex, although occasional areas of destruction were also observed in the fourth layer of the parietal lobe as well as in the deeper layers. The degeneration and destruction affected predominantly the small ganglion cells. The caudate nucleus was considerably atrophied and flattened out, but the large as well as the small cells in it were fairly well preserved. In contrast to this, the putamen was very poor in cells; the small cells had practically disappeared and the large cells were markedly degenerated. The entire brain was relatively free from cellular lipodystrophy. The cells in the pallidum and thalamus were also affected, but not nearly as severely as those in the striatum. The degenerative process in the cerebellum was very severe; here, whole rows of Purkinje cells had disappeared and those remaining showed swollen dendrites. Extensive cellular lesions were also observed in the granular layer, but the dentate nucleus seemed to have been affected most severely. The glial reaction was strikingly within normal limits; only here and there was there evidence of pathologic glial formation. In spite of the patient's age, the arteriosclerotic changes in the vessels, in general, were not unusually severe; they consisted of a thickening of the middle coat and occasional homogenization and dilatation of the adventitia. Only in a few vessels in the putamen were calcification observed in the middle coat with corresponding areas of disintegration of tissue; these were most advanced in the most ventral portion of the putamen. Finally, some of the walls of the vessels had abnormal ganglion cell-like formations either within them or attached to them. The ependyma was very thin, and there was considerable hydrocephalus. There were no evidences of inflammation anywhere.

Case 2 was that of a woman, aged 76, in whom chorea had developed two years before admission to the hospital and had lasted for twelve years. The choreiform movements involved chiefly the head and both upper extremities, the left more than the right. As this patient presented psychic disturbances during the later years of the illness, most authors would probably include this case in the group of Huntington's chorea. The psychic disturbances, however, were not

progressive, and resembled those of presbyophrenia; she had good days and bad days, and the nature of the mental symptoms could well be accounted for by senility. The brain did not show a striking substratum for such mental disturbances. The condition of the cells was that usually observed in senile brains; no senile plaques were found. There was evidence of a more or less chronic edema of the cortex, which may perhaps account for the peculiar mental picture. Tokay is therefore inclined to consider the case as one midway between a focal and a degenerative chorea. In this case, however, the significant histopathologic change was an involvement of both striata, which was more marked on the right side. Whereas the posterior portion of the caudate nucleus appeared relatively normal, its head and ventral portion were severely affected. The changes in the latter consisted: (1) of a more chronic destruction of the cells, especially the small cells, and (2) of a severe degeneration of the large cells and glial proliferation. In addition, on the right side, there was a severe, though less chronic, softening of almost the entire head of the caudate nucleus and adjacent portions of the putamen, and another focus of softening in the internal capsule that involved almost one fourth of the frontothalamic system. Since the choreiform movements were definitely more severe on the left, and the focal lesion was more marked on the right, the correlation between the two is obvious. The author, however, does not know what rôle the frontothalmic system played in the symptomatology of the chorea, although the fact that capsular lesions in this region do not produce involuntary movements would seem to speak against the theory that the frontothalamic system has anything to do with the production of involuntary movements. In the absence of lesions in other parts of the brain, then, the lesions in the caudate nucleus must be held responsible for the chorea. According to most authors (Vogt, Mingazzini and others), movements of the head are represented in the most oral portion of this nucleus, those of the upper extremities in the mesial portion and those of the lower extremities in the caudal portion. In the case cited, the distribution of the choreic movements can be readily correlated with that of the predominating lesion in the most oral portion of the striatum

KESCHNER, New York [ARCH. NEUROL. & PSYCHIAT.].

A CASE OF A TERATOID TUMOR OF THE HYPOPHYSEAL REGION. G. J. DU MARCHIE SARVAAS, Frankfurt. Ztschr. f. Path. **40**:210, 1930.

In a boy, 12 years of age, a tumor was found in the region of the sella turcica. The tumor, which extended through the nares to the outside, had led to an open communication between the orbit, the nasal cavity and the cranial cavity. The hypophysis could not be made out. The tumor was connected, however, with the infundibulum of the hypophysis. Histologically, it consisted of connective tissue, glia fibers, which contained pigment, bone, cartilage, blood vessels, fat tissue, smooth muscle fibers, different types of epithelium, nervous tissue and embryonal tissues. Besides the tumor, autopsy revealed an atrophy of the thymus and both suprarenals. The author believes that this tumor should be classified among the teratomas rather than as an epignathus because of its location, because of the absence of any parts of well developed organs, such as extremities, and because of the tumor-like growth. The relation of the tumor to the hypophysis was not studied because the hypophysis could not be located.

SAPHIR, Chicago [ARCH. PATH.].

MALFORMATION OF THE BRAIN WITH HYDROCEPHALUS AND PORENCEPHALUS. I. WERTKIN, Frankfurt. Ztschr. f. Path. **40**:571, 1930.

A case of malformation of the brain is reported in a boy, aged 15 weeks. The largest portion of the cerebrum was replaced by a clear liquid. Only the lower and posterior portions of the left hemisphere were present. The right hemisphere

was almost completely converted into a saclike cavity filled with a clear liquid. The corpus collosum was not present. The anterior portions of the left hemisphere showed outspoken microgyria. In the region of the boundaries between the right temporal, occipital and parietal lobes there was a depressed area measuring from 2 to 3 mm. in diameter, from which the sulci and gyri radiated in various directions. The corpora quadrigemina and the sylvian aqueduct were partly absent. The fourth ventricle was not dilated. The superior vermis of the cerebellum was not present. The branches of the vessels ran superficially and did not extend into the fissures. There were two central canals found in the region of the medulla oblongata. The hydrocephalus is explained on the basis of an atresia of the sylvian aqueduct. The various possibilities leading to these malformations are discussed.

SAPHIR, Chicago [ARCH. PATH.].

PROPHYLAXIS OF ACUTE POLIOMYELITIS. E. MORO, Klin. Wchnschr. **9**:2383 (Dec. 20) 1930.

Moro refers to the observation that the blood of convalescent patients and of most adults has antiviricidal power. Such blood might be expected to have prophylactic value against the disease. Since convalescent blood is rarely available in sufficient amounts for prophylactic purposes, he recommends the injection of 20 cc. from one of the parents to children under 5 years at intervals of four weeks through the period of the disease. He thinks that in large cities the injection of blood from one adult would probably give sufficient protection and that nearly all persons over 15 years of age are practically immune. In rural sections where only about 50 per cent of the adults possess antiviricidal power in their blood, it would be necessary to use mixed blood, taking it either from both parents or from adults living in cities.

SILVERMAN, Syracuse, N. Y.

A NEUROLOGIC AND ETIOLOGIC STUDY ON ONE THOUSAND MENTAL DEFECTIVES. E. J. LARSEN, Acta psychiat. et neurol. **6**:37, 1931.

Larsen studied the history and present status of 1,000 mental defectives. He classifies his material as follows: A. Endogenous mental deficiency (762 cases): (1) mongolism, 63 cases; (2) myxedema, cretinism, 9 cases; (3) dysendocrine conditions not covered by (2), 15; (4) microcephaly, 28; (5) mental deficiency, in which there appears to be a hereditary disposition although there are no neurologic-somatic symptoms, 647 cases. B. Exogenous mental deficiency (238 cases): (1) hydrocephalus, 15; (2) organic cases, i. e., patients with neurologic symptoms that are not attributable to ordinary organic nervous diseases, 223 cases.

Among the mongolian idiots he found a number of exceptions to the classic dogmas—9 first born children, 2 only children, an instance of a mongolian idiot born of a mother only 23 years of age and an instance of 2 mongolian idiots in one family. The percentage of cases showing dysendocrinism (2.4) is lower than those reported by other authors (Szondi 33, Eisenberger 29). In 46.8 per cent of his cases of mental deficiency without associated neurologic somatic signs Larsen found a hereditary predisposition to mental deficiency. In contrast to this, the exogenous group showed this disposition in only 9.2 per cent. In this connection he points out that certain mental defectives show progressive neurologic-somatic signs. This may be the result of a degenerative process that is progressive after birth, resulting in premature senility of the organism. The histories of some of the families in his cases seem to indicate a hereditary factor that is lethal to certain children—i. e., they are stillborn or die at birth—and sublethal to others—i. e., they show progressive neurologic-somatic degenerations. As an etiologic factor in mental deficiency, syphilis may be said to be of relatively slight importance. As an etiologic factor in the exogenous cases he discusses birth injury; 22.3 per cent of this group showed a history of a birth injury. In 14 cases the delivery was accomplished with forceps; in 12 the child was born

prematurely; in 16 parturition was protracted; version and extraction were done in 4 cases; asphyxia was present in 15 cases; a solution of pituitary was employed in 2 cases, and in 4 cases the child was in such a bad condition immediately after birth that it was not expected to live. In contrast to this, birth injury occurred in only 4.9 per cent of the endogenous cases. The author points out that while birth injury is an important etiologic factor in mental deficiency, particularly in the more pronounced forms of the condition, it is not as important a cause as the hereditary predisposition.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

XANTHOMATOSIS WITH CRANIAL DEFECTS (SCHÜLLER'S DISEASE). FREMANN-DAHL and FORSBERG, Norsk mag. f. lægevidensk. **92**:523, 1931.

In the form of xanthomatosis called Schüller's disease the xanthomatous infiltrations on the inner side of the cranium lead by pressure atrophy to the destruction of bone. In a girl, aged 14, with a history of trauma against the left temple at the age of 5, attacks of pain in the left temporal region set in three years later, which gained in frequency and intensity, and were followed by symptoms of slowly increasing intracranial pressure, together with diabetes insipidus, exophthalmos (left) and retardation of growth. Roentgen examinations showed the development of numerous sharp defects in the cranium, localized especially in the squamous portion of the temporal bone and also in the anterior part of the skull and left orbit, and revealed a typical maplike skull (Schüller). The diagnosis of xanthomatosis was supported by a negative Wassermann reaction, the presence of Bence-Jones protein in the urine, and by high blood cholesterol, pointing to a disturbance in the lipoid metabolism.

[ARCH. PATH.].

PSYCHOPATHY IN FEEBLE-MINDEDNESS. A. WIMMER, Ugesk. f. læger **92**:1154 (Dec. 4) 1930.

Wimmer rightly warns against a false psychiatric terminology, particularly in civil and criminal proceedings in which psychopathy is often confused with feeblemindedness. The latter condition is differentiated by degrees into idiocy, imbecility and "debility" (moron). Idiocy, according to the author, represents grades of intelligence from zero to 30 per cent of normal, imbecility grades from 30 to 55 per cent, and "debility" those from 55 to 75 per cent. Psychopathy is, in general, a constitutional deficiency which shows itself chiefly in abnormal feeling and behavior reactions, without actual defect in intelligence. It comprises peculiarities of character and variations of reaction more than anomalies of understanding and comprehension. Although psychopathic persons may have weakness of judgment dependent on false representation and feeling reactions, this weakness is purely secondary to an affective deficiency.

HART, Greenwich, Conn. [ARCH. NEUROL. & PSYCHIAT.].

Diseases of the Eye

HETEROCHROMIA OF IRIDES AND HAIR. R. W. B. ELLIS, Proc. Roy. Soc. Med. **24**:1057 (June) 1931.

The author reports a case of heterochromia of the irides and hair in a boy aged 7 years.

WILLIAMSON, New Orleans.

INJURIES TO THE EYES AT BIRTH. M. S. WENGER, Nourrisson **19**:180 (May) 1931.

Injuries to the eyes of the new-born infant may occur during normal delivery as a result of the application of forceps or from some other obstetric maneuver.

The most frequent cause is a forceps injury, and two such cases are reported. Both patients had permanent opacities of the cornea as the result of scars. The literature is reviewed in some detail.

McCLELLAND, Cleveland.

CONGENITAL HORIZONTAL NYSTAGMUS IN TWINS. P. SIVELLI, Riv. di clin. pediat. **29**:648 (Aug.) 1931.

The author reports the cases of identical twins, 7 years old, who were born with horizontal nystagmus. Forcible closing of the eyelids inhibited the nystagmus. There was no labyrinthine disturbance. No evident anatomic lesion of sight or fixation was present. There was no history of syphilis. The Wassermann reaction was negative. The parents were healthy and not alcoholic. The children were otherwise healthy, although mentally a little retarded. The lesion is probably cerebral and referable to an imperfect ovum.

HIGGINS, Boston.

ANOMALIES OF REFRACTION IN CHILDHOOD. J. BOCK, Wien. klin. Wchnschr. **44**:390 (March 20) 1931.

The anomalies of refraction in children are for the most part determined objectively with the help of glasses. The methods consist in paralyzing accommodation with atropine or homatropine, accompanied by objective skiascopy, especially the cylinder skiascopy of Kramer and Lindner, and then making subjective tests with Snellen charts, taking into account the ciliary muscle tonus. This method is essential in myopia in order to prevent overcorrection and to discover the so-called "pseudomyopic" patients. Hypermetropes should always be examined under atropine because of their great amount of accommodation. Because of the changes in children's eyes, a yearly examination should be made. Nearly all new-born infants are hypermetropic. Myopia occurs in children of school age, but rather than believe that close work causes the nearsightedness, the author sides with von Hippel in the hypothesis of a myopic anlage. Small degrees of hyperopia cause little or no discomfort owing to accommodative ability. Myopia is more difficult to control as near vision is not interfered with. The most difficult is anisometropia. Usually one eye is amblyopic in these cases. These patients find that glasses do not help the vision, and so remove them. Operation on strabismic patients is not considered until the age of 12 or 13 years, and it gives only a cosmetic result. The author believes that in the Vienna clinic the majority of strabismic patients are cured by the early fitting of a full correction.

MAYER, Chicago [ARCH. OPHTH.].

POSTTRAUMATIC TRANSFERENCE OF STIMULATION, OBSERVED AS CONSENSUAL INTRA-OCULAR HYPERTONY. SVEN LARSSON, Acta ophth. **9**:85, 1931.

An 8 year old child was to be operated on for alternating internal strabismus, but a slight amount of 1 per cent procaine hydrochloride and epinephrine was injected accidentally into the vitreous chamber, and immediately the cornea became hazy and the tension of the eyeball was lowered. The composition of the normal intra-ocular fluid was altered, the optic disk became blurred and the venous system was abnormally engorged. On the following day, the same condition prevailed in the injured eye, and a similar but milder change appeared in the eye on which an operation was not performed. This eye returned to normal in three weeks, whereas it took the damaged eye seven weeks to return to its normal status. The author reports this case to show that there is probably some truth in the matter that it is possible to transfer stimulation from the injured eye to that of the normal eye, and that it is manifested by a lowering of the intra-ocular pressure. This is a supplement to an article appearing in *Acta ophthalmologica* (**8**:261), 1930.

YUDKIN, New Haven, Conn. [ARCH. OPHTH.].

OCCURRENCE OF GLIOMA RETINAE IN RELATIVES OF A GROUP OF PATIENTS SUFFERING FROM THIS DISEASE. G. D. HEMMES, Nederl. tijdschr. v. geneesk. **75**:2271 (April 25) 1931.

The frequency of glioma retinae in Holland is about 1 : 34,000 among children born alive. The disease occurs mostly in isolated cases and only by exception in relatives. It occurs more frequently in first-born children than in those following.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Ear, Nose and Throat

KINGSTON SEPTIC SORE THROAT OUTBREAK CAUSES SIX DEATHS. HEALTH NEWS, (New York State Dept. Health) **7**:163 (Oct. 13) 1930.

One hundred and fifty-one cases of septic sore throat were reported, with six deaths. The epidemic was due to raw milk from one cow. Hemolytic streptococci isolated in this milk were morphologically and culturally identical with organisms secured from the patients' throats.

AIKMAN, Rochester, N. Y.

STUTTERING. SMILEY BLANTON, Ment. Hyg. **15**:270 (April) 1931.

Emphasizing the singular importance of speech in both emotional and intellectual development, Blanton warns that no child should leave school with a speech defect. As a matter of fact, between 5 and 10 per cent of high school and college students suffer from feelings of inadequacy or embarrassment in reciting. For the most part, stuttering is a symptom of inability to adjust to the group due to fear, timidity or hate. There is an unconscious inhibition against speech. Blanton reviews the theories of stammering, mentioning the hypothesis of left-handedness, the theory of imagery defect, the supposition that breathing is at fault and the psychoanalytic point of view. An approach by the latter technic leads him to believe that in many cases the stammerer is fixed at an oralerotic stage, and for illustration he cites several cases of stutterers who were inordinately fond of their own bodies. In such cases he obtains relief by "retraining the emotions and freeing the libido." Unfortunately, Blanton fails to describe the technic of performing the emotional retraining and libido freeing.

The treatment of stuttering comprises physical and mental hygiene and speech training. Mental hygiene includes the improvement of home discipline, the elimination of rivalry among siblings and the practice of child guidance generally. In school, the stuttering child should be allowed to speak without receiving especial attention because of the speech defect; the danger of other children imitating the stammerer is, Blanton believes, negligible. Speech training includes practice on vowel sounds and training in pitch volume, which he considers of questionable value, and precise phonetic training, which he considers harmful. Practice in speech by means of debates, talks and especially plays and pageants are highly recommended.

As a last word, Blanton warns against asking the stutterer to speak more slowly, to repeat his sentences or to take thought as to how his vocal organs are working.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.].

ELECTRODESICCATION OF TONSILS HARBORING MONILIA KRUSEI (CASTELLANI) AND NONVIRULENT DIPHTHERIA BACILLI. EDGAR R. MAILLARD, New York State J. Med. **31**:895 (July 15) 1931.

A patient, aged 16 years, received treatments weekly for nine weeks. Electrodesiccation, using a high frequency current varying from 250,000 to 400,000 cycles per second, was the method employed. Cultures were negative at the last treatment. The patient was able to attend her daily classes.

AIKMAN, Rochester, N. Y.

THE ACUTE EAR. ARTHUR H. NORTON, Northwest Med. **30**:330 (July) 1931.

Norton's treatment of otitis media following paracentesis is as follows: Fill the canal with 2 per cent mercurochrome-220 soluble and plug the ear with cotton. Instruct the parent to change the cotton when it is soiled and to do nothing else. The patient is kept in bed with an ice bag to the ear. Every other day the canal is thoroughly irrigated by the physician with a 1:4,000 solution of mercuric cyanide. As soon as the discharge ceases, inflation of the salpinx and vibratory massage are begun. Norton begins his incision at the posterior fold of Shrapnell's membrane and carries it to the lower border of the drum. As an instillation for catarrhal ears he uses phenol and chloral hydrate, 1 drachm (1.77 Gm.) each to 1 ounce (28.35 Gm.) of glycerin.

SCOTT, Philadelphia.

NASO-ORBITAL RELATIONS DURING INFANCY. ALFREDO ALCAINO, Arch. de oftal. de Buenos Aires **6**:55 (Jan.-Feb.) 1931.

This is a detailed anatomic study of the relations between the orbital and nasal cavities in the adult and in the child. At birth the ethmoid contains at least from two to three cells. During the first year of life it attains a height of 0.5 cm. and a breadth of from 2 to 4 cm., and contains from three to five well differentiated cells. The ethmoid acquires its complete development between the sixth and seventh years; at this age the frontal and ethmoid sinuses commence to be differentiated from the ethmoid cells, the frontal sinus being well differentiated between the seventh and tenth year and the sphenoid sinus about the twelfth year. The maxillary sinus acquires its definite form by the sixth year (orbital complications of this sinus being exceptional). The author believes that orbito-ocular complications of sinus origin in children under 7 years proceed from the ethmoid.

FINLAY, Havana, Cuba [ARCH. OPHTH.].

ISOLATED CHONDROMA IN THE BONY PORTION OF THE EXTERNAL AUDITORY MEATUS. E. LÜSCHER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **129**:63 (June 6) 1931.

Lüscher considers isolated chondroma of the external auditory meatus as extremely rare, and he therefore reports a case that came under his observation. In a boy, aged 11, who never before had had ear disease there developed an acute diffuse otitis externa. The examination revealed in the middle of the swollen, pus-filled auditory meatus a solid, reddish, polyp-like tissue cone. After the inflammatory changes had disappeared, the growth was removed and the recovery was uneventful. Histologic examination of the tumor revealed that it was an isolated chondroma consisting of a nucleus of elastic, reticular cartilage covered with normal skin. The author reviews similar reports from the literature, and he expresses the opinion that in some instances these formations are true neoplasms, in other cases, however, and also in the one observed they are congenital deformities which, in analogy with the tags of skin with a cartilaginous nucleus near the pinna, may be considered as a product of the first branchial arch.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

BACTERIOLOGIC OBSERVATIONS ON PHARYNGEAL TONSILS. B. STRUCK, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **129**:95 (June 26) 1931.

Struck reports the results of bacteriologic tests that were made on the tonsils of seventy-one patients at the university clinic for otorhinolaryngology in Munich. The persons on whom the tests were made were chosen at random, without consideration of sex, age or symptoms. The author gives a short report of each case indicating the person's age, the complaint, the appearance of the tonsils, the result of the examination of the smear and the results of the bacteriologic culture.

In the conclusion, he states that in the investigations on the seventy-one patients Streptococcus viridans was the micro-organism most frequently found. Numerous reports in the literature likewise name this streptococcus as the one most frequently detected in tonsillar smears. Only Richardson found more often staphylococci than streptococci. Reichenmüller, Anthon and several authors, who were mentioned by Anthon, observed a relatively frequent occurrence of Streptococcus hemolyticus. The author, however, observed the hemolytic streptococcus only once in pure culture and seven times in the mixed culture. He further states that according to Anthon's opinion the hemolytic streptococcus plays an important rôle in acute tonsillitis, and several other workers think the same, but Streptococcus viridans seems to be most frequently present in chronic tonsillitis. The question of the occurrence of the hemolytic streptococcus in scarlet fever is not entirely clear as yet, but that it is present frequently, almost exclusively in scarlet fever, has been stated repeatedly. Of special interest is the presence of fusiform, rod-shaped micro-organisms with spirilla. The author detected them in five cases with the typical bacteriologic aspects of Plaut-Vincent's angina. The anamnesis of these patients revealed throat ailments and relapsing tonsillar disturbances. The inspection of the pharynx revealed chronic inflammation. The tonsils had deep crypts and were reddish or hypertrophied. Quite frequently there were plugs and fluid secretions. But although these five patients showed the bacteriologic aspects of Plaut-Vincent's angina with the clinical aspects of chronic tonsillitis, there were no clinical signs of Plaut-Vincent's angina. Three of the patients had subjective complaints; two were entirely free from them.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

MACULA UTRICULI ACCESSORIA IN HUMAN BEINGS AND OTHER CONGENITAL DEFECTS OF THE INTERNAL EAR. J. FISCHER, Monatschr. f. Ohrenh. **65**:517 (May) 1931.

Fischer begins his article by stating that congenital defects of the internal ear which do not impair its function are little known, and that in human beings they are rare. He then reviews the reports of several other authors as well as his own on such defects in animals and in human beings. All forms of congenital defects of the internal ear that have been reported were found mainly in the medial, the bottleneck, portion of the utriculus and in the lateral wall of the sinus utricularis inferior. However, interesting, atypical epithelium formations on the macula utriculi of human beings have not been described as yet. The author had the opportunity to observe a large defect which involved the macula utriculi and the adjoining wall of the utriculus. The specimen was from a man, aged 28, who had died of pneumonia. The clinical history reveals that the patient had never been subject to ear disease. In order to explain the peculiarities of the case the author describes the results of the histologic examinations. He studied 160 sections. Following a classification of the results of these histologic examinations he evaluates the peculiar observations. The formation, in the bifurcation of the bony frame, of the tympanic membrane with its bony apophysis directed toward the chorda was atavistic. It occurs in many mammals. The unusually large ridges in the hypotympanum are known, but in the degree in which they appeared here, they may be considered as rare. The bullous thickening on the tendon of the tensor tympani was likewise an atavistic formation. The membrane that occluded the approach to the secondary tympanic membrane was a rest of the embryonal mucous tissue in the tympanic cavity. The bone fissures were larger and more numerous than is usually the case. The bony cochlea was delicate. The lamina spiralis ossea secundaria was unusually wide and thin; in one place it appeared dehiscent. There was also a dehiscence in the facialis canal, and the fasciculation of the facialis was likewise abnormal. The endolymphatic protuberances on the semicircular canals were unusually numerous. The cyst formations on the membranous semicircular canals as well as the spherical inclusions in the epithelium of the cristae were likewise variations. In the pars superior as well as in the pars

inferior there were atypical places in the epithelium characterized by a circumscribed absence of the hair cells, as the result of which the supporting cells were closer together. However, the most noteworthy defect involved the macula utriculi. The malformation consisted of two folds. They were so arranged that from the large utriculus cavity a smaller cavity was cut off by a circular wall. Considering the structure of the fold, it belonged to the macula utriculi and for this reason the author designates it as the macula utriculi accessoria. The neuro-epithelium of the macula utriculi accessoria merged into the epithelium of the macula utriculi and extended a little further into those portions of the fold which emerge from a small elevation of the utriculus wall where there are no terminations of nerves. Other malformations in the utriculus were: nodules on the medial wall, consisting of epithelium and of perilymphatic connective tissue cells, atypical sites in the epithelium and cystic cavities filled with supporting cells and with exudate. The perilymphatic tissue of the other utriculus wall appeared more strongly developed. In the sacculus there was a ridgelike endolymphatic elevation. The macula sacculi was unusually large. The ductus and the sacculus endolymphaticus showed many variations. The circumscribed atrophy in a portion of the cochlear canal, the abnormalities in the blood vessels of the stria vascularis, the atrophy at the base of the stria and the absence of the vas prominens in the upper portion of the cochlea were likewise congenital anomalies. In conclusion the author states that there is no other report in the literature of a case with such marked congenital defects of the internal ear, which apparently did not impair the function. He considers the macula utriculi accessoria as an atavistic formation. So far as the possibility of a physiologic function is concerned, he considers it comparable to the lagena, even if topographically it has nothing in common with the macula lagenae.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

THE TONSILS IN CORRELATION WITH THE THYROID. JASTREBOWA, Monatschr. f. Ohrenh. **65**:576 (May) 1931.

In order to determine the influence of tonsillectomy on the thyroid, Jastrebowa performed experiments on young pigs. On the basis of her observations she reaches the following conclusions: 1. The growth of young pigs that have undergone tonsillectomy is retarded in comparison with that of control animals in which the tonsils have not been extirpated. 2. Tonsillectomy causes marked changes in the tissues of the thyroid. 3. Removal of the tonsils causes changes not only in the tonsillectomized animals themselves but apparently also in their offspring, in the form of congenital weakness and changes in the thyroid. 4. Observations on two animals indicated that resistance against infection is weakened even by partial tonsillectomy. The author concludes that the results of these experiments justify the negative attitude of their clinic toward tonsillectomy. They consider that it is not an indifferent intervention and that it is therefore inadvisable except when special indications exist, as, for instance, in case of neoplasms.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

DEVELOPMENT OF ENDOCRANIAL COMPLICATIONS AFTER TONSILLITIS AND PERITONSILLITIS. E. WESSELY, Ztschr. f. Hals-, Nasen- u. Ohrenh. **28**:167 (May 26) 1931.

Wessely first directs attention to the reports of other authors as well as to his own previous investigations and observations on the development of endocranial complications after tonsillar processes. He mentions particularly the tests on corpses which he conducted several years before. By making injections of india ink into the peritonsillar tissues shortly before death, he had noted the transmission of the india ink through the spatium parapharyngeum up to the foramen ovale. This route seemed to be best suited anatomically on account of the looseness of the connective tissue, and it also explained all symptoms on the part of the musculature and the nerves. In the main part of the article the author gives

several new case reports and describes the results of his studies of these cases. In order to make a detailed study of the route of infection in one case he removed at autopsy a frontal block consisting of the left tonsillar region, the corresponding portions of the mandibula and of the base of the skull, prepared it for histologic examination and examined 280 sections. After describing the results of his studies he states that the process was a phlegmon with perforation into the venous system. The inflammatory spreading took place in the anterior portion of the pharyngeal space upward, and attained its strongest development at the base of the skull. Here the pterygoid muscles and the loose connective tissue of the spatium parapharyngeum contained abscesses, and in portions they were destroyed. From the anterior edge of the internal pterygoid muscle the process was transmitted by suppuration along the branches of the trigeminus and also along the middle meningeal artery, through the foramen spinosum, into the middle cranial fossa. This is the route which seems predestined by the loose connective tissue and by the direct transmission along the nervous and arterial channels. This case is typical and many other cases are similar to it. However, another case described by the author represents apparently an entirely different type. In this case there existed a peritonsillar abscess, which did not perforate into the mouth, but eroded the pharyngeal wall. During a fever-free interval a second abscess formed, which spread in the direction of the least resistance, namely, cranialward. The inflammatory irritation of the nerves caused toothaches and later trigeminus neuralgia. On the other hand, in the plexus pterygoideus, veins became thrombosed, eroded and infected, and gradually a retrograde thrombosis of the cavernous sinus developed with typical ocular symptoms. However, the fully developed pathologico-anatomic aspects in this instance were similar to those observed in the other case, only the course of the development was much slower and the temperatures were lower.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

STENOSING MALFORMATION OF THE LARYNX: THREE CASES. K. SCHRÖDER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **28**:182 (May 26) 1931.

The first case described by Schröder concerns a nursling. When 11 weeks old the infant was brought to the clinic with stridor, dyspnea and cyanosis. It was stated that stridor and dyspnea had existed since birth and that the infant had never cried and could not swallow right. To overcome the dyspnea a tracheotomy was done, but the child died on the following day as the result of pneumonia. Autopsy revealed bilateral bronchopneumonia, an insufficient development of the lungs, probably as the result of the inhibited respiration, and, besides the stenosis of the larynx, a stenosis of the right ureter. Careful examination of the larynx revealed that the rima glottidis, with the exception of a small opening at the lateral wall, was entirely closed. Histologic examination revealed that the tissues which formed the closure consisted of the fused cricoid cartilages, muscles, mucous glands and fat tissues. A second case of malformation of the larynx, which differed from the first one only in degree, concerned a man, aged 23. The patient stated that he had been hoarse since childhood and that he had difficulty in breathing. Examination revealed that the rima glottidis was two-thirds closed, apparently by a fusion of the vocal cords. A laryngofissure was done and the coalescence was divided in the direction of the rima glottidis. The author describes other details of the operation, and states that at first the patient's voice was hoarse, but the breathing was much freer; a year after the operation, the patient was able to take part in strenuous athletic activities and his voice was normal. After discussing the probable embryonal causes of these malformations of the larynx the author gives a third case report concerning a woman, aged 53. She had severe dyspnea and stated that she had never had a clear voice. She had had severe attacks of dyspnea twice before, once during childhood and once at the age of 40. A renewed attack now induced her to consult a specialist, who detected a cyst which closed the opening of the larynx almost completely and which was attached to the right aryepiglottic fold. Repeated incisions yielded first a mucous

fluid and later a suppurative fluid. However, the opening always closed again and the cyst refilled. The patient was therefore sent to the clinic for the purpose of a more radical operation. The author describes the operation and states that the patient died several days later as a result of pneumonia. He discusses the results of the histologic examination of the larynx, and in the conclusion he points out that a different surgical method might have prevented postoperative pneumonia and the death of the patient. He thinks that for the removal of a cyst, with a location like that in the reported case, von Hippel's operation for an infected intralaryngeal sac would be advisable.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

EXPERIMENTAL INVESTIGATIONS ON THE ELECTIVE LOCALIZATION CAPACITY OF TONSILLAR BACTERIA. E. WIRTH, Ztschr. f. Hals-, Nasen- u. Ohrenh. **28:** 189 (May 26) 1931.

Wirth points out that Rosenow's theory of the elective localization capacity of bacteria, if corroborated, would be of great significance for the recognition of relations between the tonsils and systemic diseases. He tested rabbits for the elective localization capacity of the tonsillar bacteria of twenty-nine patients with various systemic diseases. In all, 141 rabbits were inoculated with tonsillar bacteria. In most cases two or three rabbits were given an intravenous injection of from 0.5 to 2 cc. of a fresh suspension of tonsil pulp, and two or three other animals were given an injection of from 0.5 to 2 cc. of a mixed bouillon culture. Macroscopic and bacteriologic examination of the 141 rabbits revealed articular changes in 43 per cent, bacteria in the blood in 30 per cent, exudate in the abdominal cavity in 30 per cent, albuminuria in 21 per cent, intestinal changes in 12 per cent, splenic tumor in 10 per cent, changes in the lungs in 9 per cent, gastric disorders (generally ulcers) in 8 per cent, disorders of the liver in 5 per cent, endocardial changes in 4 per cent, pericardial changes in 4 per cent and changes in the appendix in 2 per cent. A difference in the outcome of the animal experiments when bouillon with liver or Rosenow's dextrose-brain bouillon was used could not be detected. In fifteen cases of articular rheumatism, the result of the inoculations for detecting elective localization was: positive nine times, questionable three times and negative three times. In three cases of sepsis the results were positive twice and negative once; in six cases of nephritis, questionable three times and negative three times. In three cases of endocarditis, in one case of appendicitis and in one case of cholecystitis an elective localization capacity of the tonsillar bacteria was not demonstrable. It was never possible to produce in the animals symptoms similar to those of nephritis in human beings. Marked differences in the percentile involvement of the various organs could not be detected in the different groups of systemic diseases. For instance, the joints of the rabbits inoculated with bacteria from patients with articular rheumatism showed changes in 43 per cent, and those inoculated with bacteria from patients with nephritis, changes in 39 per cent; in those inoculated with bacteria from patients with other systemic diseases articular disorders developed in 42 per cent. Thus the author's experiments speak against a marked elective localization capacity of tonsillar bacteria, as was asserted by Rosenow. However, it could be observed that bacteria from different tonsils actually have a varying tendency to attack certain organs. The frequently demonstrable arthrophilia of the tonsillar bacteria and of their toxins is especially noteworthy. Arthrotropic tendencies are noted most frequently in hemolytic streptococci, less often in other forms of streptococci, in pneumococci and in anaerobic, gram-negative bacteria. The bacteria in acute tonsillitis show generally a more marked arthrophilia than those in chronic tonsillitis. These observations make it appear probable that arthrophilic tonsillar bacteria are a causal factor in articular diseases that develop in the course of acute or of chronic tonsillitis, irrespective of the eventful existence of a specific causal agent for the real "rheumatismus infectiosus."

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

Diseases of the Skin

URTICARIA PAPULOSA: A CLINICAL, SEROLOGIC AND CHEMIC INVESTIGATION. E. F. CORSON, H. H. PERLAMAN, A. D. WALTZ and R. ASH, Arch. Pediat. **48**:349 (June) 1931.

The authors studied thirty-one cases of urticaria papulosa in an effort to shed some light on the etiology of this not uncommon condition. A careful history as to diet was obtained in each instance. Each patient was tested by the scratch method for food sensitivity. Twenty-one patients reacted negatively to all skin tests. Three reacted markedly to egg, and one showed a slight reaction. Four reacted to cow's milk and one to cheese. In only one instance did omission of the offending food result in apparent relief. A cure appeared to result in this instance. Examination of the stool and urine and a chemical analysis of the blood were done. None of the observations suggested a theory for the cause of this disease.

WADDELL, University, Va.

IMPETIGO CONTAGIOSA NEONATORUM WITH A REPORT OF FOUR EPIDEMICS. J. J. SWENDSON and S. R. LEE, J. A. M. A. **96**:2081 (June 20) 1931.

The increased incidence of impetigo contagiosa neonatorum has become a serious problem in hospital nurseries in this country and abroad. Sporadic cases are practically impossible to prevent. It is necessary to practice constant vigilance for the detection of pyogenic infections in attendants and patients and a nursery technic to prevent the development of pyodermic infections in new-born infants. In the presence of an epidemic a "three nursery system" with a separate nursing personnel for each nursery should be established. The first nursery is the one in which the cases originally develop. The second one should care for the cases that have been removed from the first nursery and the third should receive all babies born after the epidemic is discovered. The first nursery should not be used again until the last baby has been discharged, the nursery cleaned and a new personnel established. Active treatment consisted of opening each vesicle, painting the base with 5 per cent silver nitrate and applying Taylor's dusting powder.

BONAR, Salt Lake City.

ETIOLOGY OF ACRODYNIA: REPORT OF THREE CASES. WILLIAM WESTON, JR., South. M. J. **24**:378 (May) 1931.

The author reports three interesting cases of acrodynia. He is of the opinion that acrodynia is primarily a deficiency disease with a superimposed infection. In the three cases reported, the patients recovered without having had tonsillectomies, and in only one of the three cases were diseased tonsils observed. Infection occurs easily in these patients, usually being found in the nasopharynx. The author believes that the infection has a synergistic action on the symptoms of the disease.

SCHLUTZ, Chicago.

THE EFFECT OF HEAT ON AN ERYTHEMA PRODUCED BY ULTRA-VIOLET IRRADIATION. LEONARD HILL and H. J. TAYLOR, Brit. J. Physical Med. **6**:25 (May) 1931.

The object of the work was to decide whether heat applied before, during or immediately after ultraviolet radiation has any effect on the latent period and the intensity of the resultant erythema. A Hanovia air-cooled quartz mercury vapor lamp was used. The infra-red radiations of wave length longer than 14,000 angstrom units were filtered out by interposing a quartz vessel filled with distilled water. When radiant heat was employed in addition, the sources were carbon filament or incandescent gas lamps.

The authors found that radiant heat has little effect on a mild erythema. It seemed that there was some tendency to reduce the erythema and increase the

latent period, but the effect was considered negligible. In the case of a stronger erythema, radiant heat seemed to lengthen the latent period, but increase the intensity of the erythema. The effect was small but definite. No effect was noticed when the skin was irradiated at the same time as it was heated. A skin irritant such as a mustard plaster, increased the ultraviolet erythema to a marked extent, whether applied before or after the irradiation; the latent period, however, was lengthened. It was pointed out as interesting that the latent period may be lengthened while the resultant erythema is somewhat more intense.

HARTMAN, Cleveland.

HEREDITARY ECTODERMAL DYSPLASIA. JEAN SMITH, Proc. Roy. Soc. Med. **24**:323 (Jan.) 1931.

A boy, aged 13 months, was brought to the hospital because of his resemblance to an older brother. The chief characteristics were: (1) peculiar facies, (2) sparse fair hair, (3) dilated scalp veins, (4) thick everted lips, (5) a depressed nasal bridge, (6) large projecting ears, (7) absence of sweat glands, (8) dental abnormalities as shown in a roentgenogram and (9) a tendency to attacks of high pyrexia unassociated with any constitutional disturbance. On the eleventh day after birth, his temperature reached 108 F., although the only explanation found for it was possibly too much clothing.

WILLIAMSON, New Orleans.

URTICARIA PIGMENTOSA. G. L. HALLEZ, Nourrisson **19**:106 (March) 1931.

Urticaria pigmentosa was first described by Nettleship in 1869. It occurs most commonly in infants aged less than 1 year, and has even been observed in newborn infants; 282 cases have been collected from the literature; 82 per cent were in infants under 1 year of age. A case is described that occurred in a Mexican baby girl 9 months old. A biopsy showed a thin epithelium and groups of mast cells just under the epidermis with a large quantity of light brown pigment resembling melanin in the malpighian layer. Around the blood vessels were oval and fusiform cells with chromatin-containing nuclei. Reference is made to an article by Kiyasu (AM. J. DIS. CHILD. **38**:1020 [Nov.] 1929). No effectual treatment has been found.

MCCLELLAND, Cleveland.

GANGRENE OF THE GENITAL ORGANS FROM EDEMA DISTENTION IN LIPOID NEPHROSIS. R. C. AGUIRRE and E. J. SANBIDET, Rev. de especialid. **5**:1665 (Nov.) 1930.

The authors present a case of lipoid nephrosis in a boy aged 2 years in whom, after a severe generalized edema, gangrene of the genitals developed. Reduction of the edema improved the condition. The case is well illustrated.

SANFORD, Chicago.

SARCOMA OF THE SEPTUM. A. R. LAMBRINI and J. MADERO, Rev. de especialid. **5**:1845 (Nov.) 1930.

An 8 year old boy suffered from a nasal obstruction for five months, At operation a tumor mass was removed, which was found to be a sarcoma.

SANFORD, Chicago.

THE HERPES-ZOSTER-VARICELLA PROBLEM. H. MOMMSEN, Monatschr. f. Kinderh. **50**:11 (May) 1931.

This is an interesting report of epidemics of herpes followed in the usual incubation time by varicella. In three epidemics a case of zoster was followed in the second generation by zoster affecting the sister of the previously sick child and by

nine cases of varicella. In the fourth generation one case was noted apparently combining the two diseases, and in the fifth generation varicella appeared again. The author concludes from these clinical studies that the varicella virus is changeable and by incubation in certain carriers, may give the picture of herpes.

GERSTLEY, Chicago.

CASE OF UNILATERAL BRAIN AND SKIN HEMANGIOMA. WERNER SCHAEFER, Monatschr. f. Kinderh. **50**:35 (May) 1931.

The author reports a case in a 1 year old baby, including photographs and a roentgenogram of the skull. The child suffered from a unilateral extensive hemangioma involving much of the left part of the body. The development of severe nervous symptoms led to having an encephalogram made. On the basis of this picture the author also diagnosed a hemangioma of the brain.

GERSTLEY, Chicago.

SERUM ALBUMIN ERYTHROCYTES AND BLOOD WATER IN ERYTHRODERMIA DESQUAMATIVA. H. SCHOENFELD and L. BLADT, Monatschr. f. Kinderh. **50**: 130 (June) 1931.

In the florid stage of erythrodermia desquamativa there is regularly a diminution of serum albumin. This returns to normal during convalescence. This diminution is unquestionably an actual one and has nothing to do with the almost constant increase in blood water. The latter, on the other hand, appears to be relative, induced by the almost constant anemia.

GERSTLEY, Chicago.

UNSPECIFIC SKIN REACTIONS. OTTO TEZNER, Monatschr. f. Kinderh. **50**:160 (June) 1931.

In a study of skin reactions during various allergic processes, such as measles, phenylethylhydantoin (nirvanol) sickness, serum sickness and vaccination, the author finds that all other allergic reactions, such as the Dick, Pirquet and specific serum reactions are influenced in a positive or negative manner. Strict toxin reactions, such as the Schick, are not affected. The author cautions against the interpretation of any of the allergic skin reactions if the patient is showing any manifestations of allergy. It is interesting to note in these experiments that there does seem to be a difference in the reactions obtained in the Dick and the Schick tests.

GERSTLEY, Chicago.

Miscellaneous

THE INFANT SKIN AND INFANTS' UNDERWEAR. DOUGLAS P. ARNOLD, Arch. Pediat. **48**:392 (June) 1931.

The results of a questionnaire submitted to pediatricians, general practitioners, nurses and hospital technicians are given and discussed. This paper is an account of how a manufacturer of infant wear, widely prescribed by physicians, cooperated with physicians, nurses and hospital and laboratory directors in carrying out a difficult, expensive and highly valuable piece of research work in a field that leading pediatricians had expressed themselves as being intensely interested in but unable to explore adequately.

WADDELL, University, Va.

PICROTOXIN AS AN ANTIDOTE IN ACUTE POISONING BY THE SHORTER ACTING BARBITURATES. A. H. MALONEY, R. H. FITCH and A. L. TATUM, J. Pharmacol. & Exper. Therap. **41**:465 (April) 1931.

Derivatives of barbituric acid are increasing in number and in use. Dangerous or fatal poisoning is not uncommon. Poisoning of rabbits and dogs by three of

the shorter acting barbiturates, amytal, pernocton and pentobarbital sodium, was successfully combated by picrotoxin; other methods and drugs failed. The authors note that previous workers had used picrotoxin successfully against chloral poisoning of rabbits.

PILCHER, Cleveland.

HEALTH RESORTS FOR DELICATE CHILDREN. CHEYROU-LAGREZE, Arch. de méd. d. enf. **34**:141 (March) 1931.

Alarmed at the enormous number of French children suffering from anemia, underweight and faulty development, the physicians of France are concerning themselves more each year with stimulating interest in seaside and mountain camps. The author outlines the relative advantages of marine resorts and of convalescent camps in high altitudes.

AMESSE, Denver.

INDICATIONS FOR AND TECHNIC OF BLOOD TRANSFUSION IN THE INFANT. E LESNÉ and G. DREYFUS SÉE, Rev. franç. de pédiat. **7**:1, 1931.

The authors discuss the value of blood transfusion in acute and chronic nutritional disturbances, blood diseases, pulmonary infections and septicemias. Its value may be due to many factors, some of which are not thoroughly understood; certainly the supplying of fluid, hemoglobin and serum antibodies has beneficial effects. The quantity recommended is 30 cc. per kilogram. The method described is one which assures success, in that a trocar with an olive-shaped bulge at the end is tied into the vein; there is no chance of this slipping out. As the superficial veins are used, many are available should it be necessary to repeat the transfusion. The usual precautions must be taken to determine the compatibility of the bloods and to exclude syphilis and malaria in the donor.

LESLIE, Evanston, Ill.

THE LOGICAL BASIS OF FAMILY ENDOWMENT. W. PLATT, Rev. internat. de l'enf. **11**:107 (Feb.) 1931.

To alleviate economic conditions connected with the advent of children in homes with small incomes, there exists in England an association known as the Family Endowment Society. This organization, of which Miss Eleanor Rathbone, M. P., is the leading spirit, has adopted the broad policy of furthering not one plan but every plan designed to assist young couples in raising children in an atmosphere of contentment, with funds sufficient to ward off the disasters to health and morals so frequently visited on the submerged tenth. France leads the world in this field; her regulations for employer's pools and independent allowances are most admirable; they seem effectually to circumvent the possibility of discrimination against men with families.

AMESSE, Denver.

PROTECTIVE LEGISLATION OF CHILDHOOD IN PORTUGAL. A. D'OLIVEIRA, Rev. internat. de l'enf. **11**:113 (Feb.) 1931.

Under the law of 1911, Portugal has three main juvenile courts presided over by individual judges and a series of auxiliary establishments in which the bench consists of a judge, a physician and an educator. In addition to the usual functions of such agencies, these courts are authorized to deprive parents of their privileges when the influence of the latter is unwholesome and to compel relatives, even remotely placed, to contribute, consistent with their means, to the maintenance of the child on trial. In families already indigent, the care of the delinquent child is assumed by the state. He may be sent to a public welfare institution or to a reformatory at the discretion of the court. In other instances, the child may be placed in a suitable family or be sent to school; certain offenders of the proper age are enrolled in the army or the navy!

Auxiliary services are available in every juvenile court; each delinquent is given a medical, a scholastic and a psychologic examination and is also interrogated by an officer from the vocational guidance bureau. The groups are divided into first offenders, second offenders and hardened repeaters; according to their classification they are recommended to foster families, are placed on probation or are sent to reformatories, of which there are two for boys and one for girls.

AMESSE, Denver.

PREVENTIVE WELFARE WORK IN DENMARK. O. SKJERBAEK, Rev. internat. de l'enf. **11**:126 (Feb.) 1931.

All measures destined to keep the child in a proper home atmosphere are grouped, in Denmark, under the term preventive welfare. They include laws dating back as long as one hundred and fifty years. For example, the provisions made at that time for the maintenance of illegitimate children are still in force. Other safeguards include the appropriation of funds by the state for families in distress, the establishment of free schools, medical services, holiday camps, etc.

Among the special services the author quotes the law on guardianship. Under this act, competent authority may first give warning to neglectful parents and, if necessary, appoint a suitable guardian, usually a woman, for children living under bad influences. In 1828, Copenhagen established its first day nursery; this was followed in succeeding years by the opening of many such institutions in the provinces. In 1874, the first manual training work was begun and in 1882, the first crèche was inaugurated. Kindergartens appeared in 1901. At this time there are in active operation, in addition to these agencies, maternity centers, work schools, play centers and holiday camps.

AMESSE, Denver.

THE STUDY AND TEACHING OF PEDIATRICS. LEONARD FINDLAY, Rev. internat. de l'enf. **11**:219 (March) 1931.

In the course of an address delivered in Belgrade before the Jugoslavian Medical Association, Findlay protested against the consideration of pediatrics as a specialty. He rather regards it as general medicine practiced during the earlier and, as he remarked, the most important years of life, at least so far as prophylaxis and cure are concerned. The ideal pediatrician is a general practitioner with a full knowledge of disease at a certain period of life, but if one wishes to set pediatrics apart as a specialty one could, with equal justification, have a special physician for adolescence, another for the prime of life and another for old age!

Such an artificial division may bring about some little increase in knowledge, but it has not especially benefited the patient and it undoubtedly has narrowed the outlook of the family doctor; it has had a serious effect on the teaching of the medical student, as shown by the fact that the things the doctor is called on most frequently to perform, the delivery of women and the care of children, are the very subjects on which least instruction is given. In the outpatient department of every children's hospital there is a wealth of material which should be better utilized. Here the student may familiarize himself with both the common and the unusual, and prepare himself for curative and for preventive pediatrics.

AMESSE, Denver.

Society Transactions

ST. LOUIS PEDIATRIC SOCIETY

Oct. 23, 1931

GUSTAVE LIPPMAN, M.D., *President*

KATHERINE BAIN, M.D., *Secretary*

NUTRITIONAL EDEMA AND DYSENTERY, WITH COMPLICATIONS. Presented by DR. MAX DEUTCH.

A boy, aged 20 months, was admitted to the Children's Hospital with the history of chronic underfeeding since the time of weaning seven months before. He had had malaria four months before admission; generalized edema had been present for three months and dysentery for ten days. On admission he weighed 16 pounds 8 ounces (7,470 Gm.), and showed marked malnutrition and generalized edema. His urine, except for an occasional faint trace of albumin, was normal on repeated occasions, and there was no evidence of cardiac disease. The serum protein was 3.7 per cent. Under the direction of Dr. A. F. Hartmann, the administration of acacia intravenously and blood transfusions resulted in the loss of about 20 per cent of the body weight and almost complete disappearance of the edema within a week. The dysentery was of the Shiga type, and persisted until the eighth week after admission. Otitis media and later mastoiditis developed while the patient was in the hospital, and he began to gain weight steadily only after mastoidectomy nine weeks following admission. Postoperative pneumonia developed, but the child recovered within a few days. Twenty days after operation his temperature suddenly rose. Measles, pneumonia, mastoiditis on the side opposite that of the first attack and lateral sinus thrombosis were eliminated before Plasmodium vivax was finally found in the blood smear, indicating a recurrence of the malaria that had first developed four months before admission and for which the patient had been inadequately treated. The fever, which after a few days was tertian, subsided promptly after the administration of quinine was begun. The child did well thereafter, weighing 19 pounds (8,620 Gm.) at the time of discharge (age, 2 years) and 32½ pounds (14,982.72 Gm.) when seen in the outpatient department six months later.

ACUTE LEUKEMIA. Presented by DR. J. V. COOKE.

A case of acute leukemia without leukocytosis in a boy aged 3 years was presented. On the patient's admission to the hospital there were skin hemorrhages, an enlarged spleen, fever and a leukocyte count of 2,500, with more than 90 per cent nongranular mononuclear cells. Following treatment with a specially prepared fraction of bone marrow there was a clinical remission with a temporary increase in polymorphonuclear leukocytes to 45 per cent. After six weeks the child was afebrile and in good clinical condition, but the blood again showed a high proportion of abnormal forms. The possibility of acute leukemia being a result of the suppression or absence of a substance necessary to the mechanism of normal blood formation was discussed.

MONGOLOID IMBECILITY: FREQUENCY, RACE AND SEX. Presented by DR. ADRIEN BLEYER.

The frequency of mongolism has been determined, the world over, from institutional figures which, because of the excessively high death rate in early life,

before institutional age, cannot represent the facts. In a group of almost 50,000 children attending the outpatient department of Washington University School of Medicine during fourteen years, 777 mentally defective patients were found, among whom there were 115 mongoloid imbeciles. This indicates that there is 1 mentally defective child for approximately 60 dispensary children. The mongoloids comprised 14.6 per cent of the mentally defective children.

The impossibility of mongolism occurring among Negroes, as maintained by Crookshank, was refuted by the finding of 8 cases among children of this race, about the same proportion as was found among the white children. Two cases were found among Jews. Mongolism in a Mexican boy, a race not included in Brousseau's list of races, was reported.

Mongolism was found more commonly among males than females, the ratio being 6.2 : 3.9, while that among mentally defective persons as a class was found to be 5.9 : 4.1. Thus sex may actually be a contributing factor.

Book Reviews

Scharlach. By Professor R. Kraus. Price, 45 marks. Pp. 335. Berlin: Urban & Schwarzenberg, 1931.

In this volume compiled by Professor R. Kraus, the author presents his theories as based on his experiments and on the experiences of his co-workers. He attributes to Streptococcus scarlatinae, the dominant pathogenic rôle in scarlet fever, and he thinks that both clinical and laboratory evidence tends to show the specificity of the organisms.

From a polemic standpoint, the volume is interesting in that it takes up in detail the reasons why so many authors have failed to substantiate the idea of specificity, the author making short shift at times of any opposition with the opinion that the work in question was not "thorough enough" or was lacking in "quantitativeness."

The world literature is reviewed, but the various points made are mostly used to bolster the author's conclusions.

The volume first calls attention to the fact that Moser, who invented the serum bearing his name, did not get the proper credit due him. Kraus admits that the Dicks were the first to demonstrate the antitoxic value and the first to devise a test (Dick) for standardization purposes, but he thinks, nevertheless, that the antitoxin should be known as Moser-Dicks' antitoxin.

The author attempts to prove specificity for Streptococcus scarlatinae in the usual way: (*a*) through agglutination phenomena; (*b*) by absorption phenomena, (*c*) by the presence or absence of the Schultz-Charlton phenomenon, (*d*) by the use of the Dick test, etc.; he finally admits that absolute proof of true specificity is not available. He very properly calls attention to the fact that Koch's postulates are not demonstrable in many recognized diseases. Koch's postulates cannot be proved since no animal is susceptible to the disease. It is thought, however, that even in the absence of this information, specificity should be admitted.

The author believes that the streptococcus causing erysipelas, sepsis, etc., may belong to the same group of organisms possessing group agglutinins, but that such a fact does not rule out specificity.

A lot of old Moser serum was found in the State Serum Laboratory at Vienna, and a difference in potency was found between various lots, thus, according to the author, explaining Moser's early failures.

In discussing the therapeutic serums, there is an attempt to show the efficacy of the serum in cutting down the death rate, and such rates as 41 per cent are noted. The author is enthusiastic about the therapeutic effects of serum treatment and remarks that "therapeutic serum is now so good that noboby would dare not give it."

In all, the volume is well written. There is a good bibliography attached, but if a reference to the literature is the only thing wanted, the reviewer does not see how it can surpass the volume on "Scarlet Fever Streptococci" released by the Pickett-Thomson Research Laboratories and compiled by the Thomson brothers.

The book contains many excellent illustrations.

Difficult Labor. By G. E. Herman. Seventh edition, revised by Carlton Oldfield. Price, $5.50. Pp. 537, with 8 radiographic plates and 197 illustrations. New York: William Wood & Company, 1929.

The material in this book has been very ably presented, especially for the student, intern or resident physician and the general practitioner.

The reader receives more definite guidance in the handling of cases of difficult labor than he gets from some textbooks of the present day. In these he is told

of many things that might be done in cases of an emergency, but he is not always clearly told which is the best.

The author's immense experience has enabled him to state definitely concerning the various obstetrical difficulties exactly which is the best of one or more procedures to follow, ever mindful of both mother and infant.

Beginning with the first chapter, in discussing normal labor, the author prepares the learner to recognize pathologic labor.

The chapters on difficult occipitoposterior positions, pelvic presentation, abnormal uterine action, contracted pelves with their complications, hemorrhage before and after delivery and the toxemias of pregnancy are particularly of value. The foregoing conditions play a rather large part in the handling of pathologic obstetrical cases. In this presentation, the author comes clearly and definitely to the point, with reasons and results to back up his opinions.

This treatise on "Difficult Labor" has not aimed at giving a full presentation of current opinions, but has rather compiled the knowledge and private experiences of the writer.

Recent Advances in Allergy. By George W. Bray, M.D. Price, $3.50. Pp. 432, with 98 figures and photographs. Philadelphia: P. Blakiston's Son & Company, 1931.

The first part of this book deals with the history, experimental observations and biochemical aspects of allergy. The factors are considered separately as hereditary, psychic, endocrine, nasal and toxic. The second part discusses the individual manifestations of allergy, asthma, hay fever, cutaneous allergy (including eczema), migraine, headache, epilepsy, food allergy, bacterial allergy and drug and serum reactions. The individual subjects are considered briefly but concisely. For example, in infantile eczema, while the different substances that may be involved in producing the allergy are discussed, the treatment is very conservative. Local treatment to the skin is given first place, and adjuvant therapy second and third. In babies sensitive to breast milk, the author does not advise weaning or investigating the mother's diet, but continuing the breast feeding. He has had success by giving both mother and child hydrochloric acid before feeding.

The book is interesting and well written. The recent development of the subject has caused so much to appear in the literature that it has become impossible for the ordinary man to keep up with the subject. This book brings the recent advances together in a readable state. At the end of each chapter is a complete bibliography.

Les lésions cérébroméningées à la naissance. By R. Waitz. Price, 40 francs. Pp. 270, with 57 figures. Paris: Gaston Doin, 1931.

A study of the pathology of cerebral lesions in the new-born is based on forty-two autopsies. The author found that cerebral hemorrhage was almost always subarachnoid. Associated with the lesions were vasodilatation, seroalbuminous edema and choroid alteration. He traces the development of repair of these lesions by excellent photomicrographs.

The spinal fluid was studied in three hundred cases. The author found that cerebral hemorrhage was shown by alterations in the spinal fluid, such as hyperalbuminuria, cellular elements and blood cells. Obstetrical factors, such as presentation, premature rupture of the membranes, rigidity of the maternal parts and injections of pituitary extract, were important in the etiology. Syphilis did not play a part in the etiology. From a direct etiologic standpoint, the condition is always a circulatory disorder caused by compression. The clinical condition should be divided into three stages: (1) that of apparent death, (2) coma for twenty-four hours and (3) secondary developments, lasting for from two to five days. The changes consist of convulsions, tension of the fontanel, vomiting and variations in temperature.

The general mortality was 18 per cent; in cases of apparent death it was 33 per cent, and in coma during the first hours it was 77 per cent. The ultimate prognosis should be guarded. The treatment is prophylactic and symptomatic. Repeated lumbar punctures seem to diminish the symptoms.

This book is concise and well written, and the illustrations are excellent.

Conferencias sobre patologia de la primera infancia. By Instituto de Clinica Pediatrica y Puericulture, Prof. Dr. L. Morquio, Director. Pp. 512, with 30 cuts and illustrations. Montevideo: Talleres Graficos de A. Monteverde y Cia, 1931.

This book contains the published articles of the program of the Institute of Clinical Pediatrics in Montevideo, in July, 1931. There are thirty-one papers on pathologic conditions in infancy, including disturbances in nutrition, respiratory diseases, blood disturbances, tuberculosis and surgical conditions. The articles are concise, complete and interesting.

Child Health and the Community. By Courtenay Dinwiddie. Price, $1. Pp. 80, with 8 photographs. New York: Commonwealth Fund, 1931.

This book is a brief review of the essential principles of the Commonwealth Fund's work in Fargo, Athens, Rutherford County, Tennessee, and Marion County, Georgia. First, the reason for this work is discussed, followed by a description of the communities studied. The last two chapters deal with the relations with the physicians and the results of public opinion. An appendix gives an outline of the detailed work of the program.

Guide to the Radiologic Diagnosis in Heart Disease. By G. Nemet. Price, 35 cents. Pp. 33, with 31 illustrations. New York: New York Tuberculosis and Health Association, 1931.

This pamphlet has been prepared by the Research Subdivision of the New York Heart Committee. It contains a description of the technic necessary for radiologic examination and a discussion of twenty-five groups of conditions, with illustrative diagrams.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

Secretary: Prof. G. Scheltema, 14a Peolstraat, Groningen, Holland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Jay I. Durand, 1305, 4th Ave., Seattle.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: New Orleans. Time: May 9-13, 1932.

American Academy of Pediatrics

President: Dr. John L. Morse, 319 Longwood Ave., Boston.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New Orleans. Time: June, 1932.

American Child Health Association

President: Hon. Herbert Hoover, Washington, D. C.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Pediatric Society

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Rochester, Minn. Time: May 26-28, 1932.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.
Place: New Orleans. Time: 1932.

Children's Hospital Association of America

President: Dr. Joseph Brennemann, 707 Fullerton Ave., Chicago.
Secretary-Treasurer: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: Fall, 1932.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.
Place: Mobile. Time: April 19-21, 1932.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.
Place: Buffalo. Time: May, 1932.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.
Place: Tulsa. Time: May 14, 1932.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. E. W. Barron, 1512 Marion St., Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

TEXAS PEDIATRIC SOCIETY

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. James A. Wood, Medical Arts Bldg., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, Medical Arts Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 625 Lowry Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Henry S. Stern, 807 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. C. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Wilford W. Barber, 227, 16th St., Denver.
Secretary: Dr. John A. Schoonover, 1616 Tremont Pl., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William M. Happ, 523 W. 6th St., Los Angeles.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.

THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is published by the American Medical Association as a means for the advancement of knowledge of the diseases of children and for the publication of scientific investigation in this field.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. Clifford G. Grulee, 310 South Michigan Avenue, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago.

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The AMERICAN JOURNAL OF DISEASES OF CHILDREN is published monthly. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75, including postage. Single copies, 85 cents, postpaid.

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